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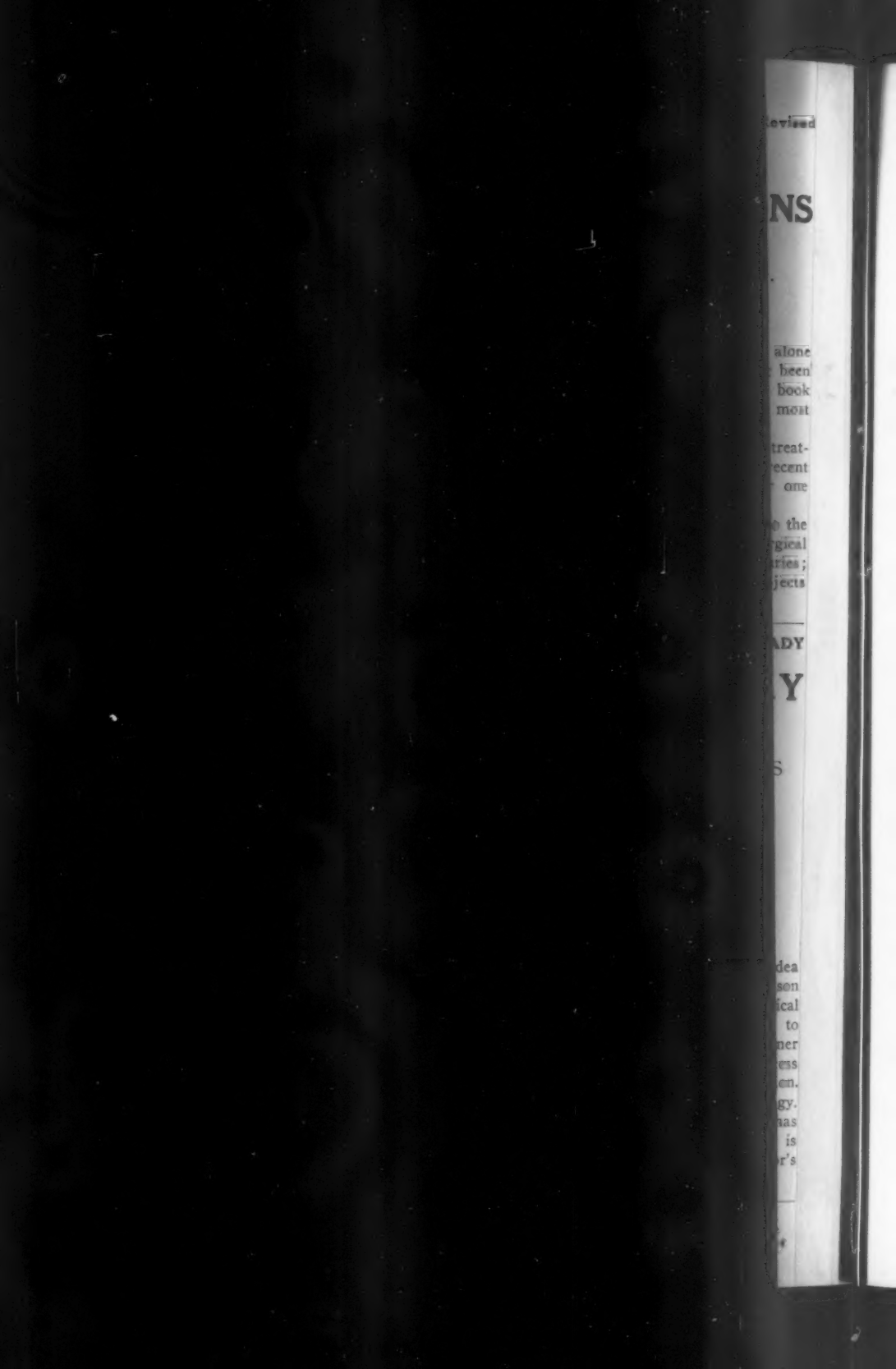

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THE

AMERICAN JOURNAL

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DECEMBER, 1912

ORIGINAL ARTICLES

PARTIAL GASTRECTOMY IN A CASE OF MULTIPLE CARCINOMA OF THE STOMACH.

By John H. Gibbon, M.D.,

PROFESSOR OF SURGERY IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Instances of multiple primary malignant growths are sufficiently rare to warrant their publication. The following case of multiple primary carcinoma of the stomach is not altogether unique, but the recording of similar conditions has been infrequent.

H. K., aged forty-eight years, was sent into my service at the Jefferson Hospital by Dr. O. L. Wingate, January 4, 1912, and gave the following history: His family history was absolutely negative, his previous personal history was also negative; he had used beer, coffee, tea, and tobacco in moderation; he had always enjoyed good health and considered himself perfectly well until June, 1911, when he first developed gastric symptoms. At that time he was suddenly seized with a vomiting attack on the street, and says that the vomited material was black, and that he thought it contained blood. Repeated similar attacks occurred through the summer, and he rapidly lost weight and color. In the fall, under treatment, he improved, vomiting ceased, and he regained some weight and color. During the two months previous to admission the vomiting returned, and there was again rapid loss of weight and color. In the four weeks prior to admission he had lost twelve pounds in weight. The interesting point in his history, in view of the subsequent findings, is that he never had any pain or symptoms of indigestion, and the slight discomfort which he felt showed no

regularity as to the time of its occurrence. His chief complaint was vomiting, which did not occur every day, but he often vomited in the evening the food which he ate at breakfast. He thought that he had vomited practically all of the food taken during the few days previous to admission. He also complained of weakness and of tiring easily.

Examination showed a thin, very pale individual of distinctly cachectic appearance. Palpation of the abdomen revealed no tenderness, rigidity, or tumor. The blood examination was: Hemoglobin, 44 per cent.; red cells, 3,140,000; leukocytes, 12,000; color index, 0.7. The gastric analysis was: Free hydrochloric acid absent; total acids, 0.0584; combined acids, 0.02185; no lactic acid; no bile; considerable blood; a few Oppler-Boas bacilli; a few yeasts; a few epithelial cells. A diagnosis of probable gastric cancer was made, and the patient was sent to Dr. Manges for *x*-ray examination. The plates showed marked irregularity in the outline at about the middle of the greater curvature and again near the pylorus in the greater curvature. The motility of the stomach was considerably interfered with, but Dr. Manges did not think that there was an obstruction of the pylorus; his interpretation of the plates was that the condition was malignant and that there were two distinct lesions.

Operation. On January 27, 1912, under chloride of ethyl-ether anesthesia, preceded by morphine and atropine, the abdomen was opened through the left rectus, and at once a large round mass at about the middle of the greater curvature was found involving both the anterior and posterior walls. The mass was densely hard, and there were small nodules beyond it; the gastrocolic omentum was puckered and attached to the growth. About an inch from the pylorus, on the greater curvature, was another hard mass, with an excavated centre, which could be easily felt through the anterior wall. The whole stomach was freely movable; there was no pyloric obstruction; no adhesion to the pancreas; no marked enlargement of the glands. The case seemed a good one for resection of the stomach, and I thought that there would be enough of the organ left for a gastrojejunostomy. The blood supply of the area to be removed was first tied off, a ligature placed about the duodenum, and a clamp placed obliquely across the stomach from a point well above the larger growth to the cardiac end of the lesser curvature. The portion of the stomach included between the ligature and the clamp was then excised; the remaining pouch of the stomach was closed with two continuous catgut sutures and inverted with a continuous suture of linen thread. As the ligature around the duodenum did not completely close it, the cut end of this bowel was closed and inverted. I was surprised to find that the larger growth was adherent to the mesocolon, and I feared at first that the transverse colon itself was involved in the growth. I

found, however, that I could trim away the adherent peritoneum without opening the bowel. The jejunum was then brought up through an opening in the mesocolon and attached to the posterior wall of the cardiac end of the stomach by catgut and linen sutures. The patient lost little blood during the operation, which occupied about an hour, and at its conclusion his pulse was 86.

The patient's convalescence was perfectly satisfactory excepting that he had a slight infection of his wound, which necessitated his remaining in bed longer than usual. He was discharged from the hospital on March 7, 1912. I saw him last on March 30, when he told me that he was able to eat all kinds of food and had no discomfort whatever. In the three weeks which had elapsed since his discharge he had gained twelve pounds. He was still pale, but his color was much better than before operation, and although I hesitated to prognosticate a cure, I felt confident further improvement would take place.

July 23, 1912: The patient died on June 19 of general debility, but without the recurrence of any gastric symptoms whatever. His only complaint was weakness in the legs, and it was thought for a time that he might have a spinal metastasis, but this could not be definitely determined. He did not die in the hospital, and no autopsy was made.

As the principal interest in this case centres in the character of the growths found, I am including a full pathological report from the laboratories of the Jefferson Hospital.

"PATHOLOGICAL REPORT, January 27, 1912. Patient H. K. Specimen, stomach. The specimen is an irregular portion of stomach wall, measuring 15 cm. in length and varying in width from 13 cm. at the broader to 7.5 cm. at the narrower end.

"The mucous surface bears two ulcers. The larger extends to within 1 cm. of the broader extremity. It is oval in outline, being 7.5 cm. long and 6 cm. wide. A peripheral zone 1.5 cm. wide is elevated from 0.5 to 1 cm. above the surface of the stomach. The surface of this raised margin is quite uneven, and has many reddish areas where the mucosa is lacking, the latter for a large part of the circumference forming only the outer wall of the elevated portion and not covering its surface.

"Internally the elevated zone dips down abruptly to the floor of the ulcer proper, which is 3 by 3.5 cm. The floor is fairly smooth and appears to be formed by the muscle coat, although this cannot be stated with certainty. Near one margin of the depression is an almost circular area 1 cm. in diameter that is much deeper than the remainder. The floor of this small area is formed by the inner surface of a grayish nodule 2 cm. in length and 1 cm. in height that is attached to the peritoneal surface of the stomach; around the nodule is a narrow irregular zone of infiltration of the peritoneum that is but slightly elevated. This nodule is quite readily separated

from a part of its attachment to the tissue surrounding the ulcer, this separation causing the appearance of an opening into the latter; apparently the escape of stomach content had been prevented only by this adherent mass, the stomach wall having a complete circular perforation 1 cm. in diameter.

"The smaller ulcer is toward the narrow end of the specimen and 1.5 cm. from the border of the large one, with which it has no demonstrable connection, either superficial or deep. It is 3.5 by 5 cm. in size, the peripheral portion being elevated as in the larger one. This elevated part varies from 0.8 to 1.5 cm. in width, and is covered by mucosa except for a few points along the narrower portion. The depressed portion or ulcer proper is 2 cm. in diameter, with a fairly smooth, grayish floor, probably formed by the muscle coat of the stomach. The peritoneal coat is slightly elevated and thickened over the area corresponding to this lesion.

FIG. 1.—Portion of stomach wall, showing the larger and smaller ulcers.

"The gastric mucosa not involved by the ulcers is rather smooth, grayish-red in color, and is markedly corrugated, especially in the vicinity of the ulcerated areas. Incision of the raised margins of the ulcers encounters decided resistance, and the cut surfaces are somewhat granular, grayish-yellow in color, and quite uniform in texture.

"Small portions of each mass were fixed in alcoholic corrosive sublimate, cleared in cedar oil, embedded in paraffin, sectioned, and the sections stained with hematoxylin, eosin, and Van Gieson's mixture.

"Histology: Sections from the margin of the smaller of the two ulcers possess a partial border of gastric mucosa, which for the greater part shows but little change other than moderate infiltration by small round cells. In the depths this cellular infiltration is more prominent, and there is a moderate increase of intertubular connective tissue. Immediately below this is a rather abrupt transition to a newgrowth which has partly or entirely replaced the muscularis mucosæ and forms the remainder of the sections. This new growth is made up of tubules, very irregular in size and shape, which are separated by bands of connective-tissue stroma that in areas is well marked, in others less prominent. The stroma is possibly residual submucosa (from its position), or is new tissue developed as a part of the growth. The tubules are lined by columnar epithelial cells, mostly in a single layer, but in some tubules stratified. These cells are placed directly upon the fibrous stroma. Some of the tubules are partly filled by granular debris or desquamated and degenerating tumor cells. The stroma shows but little cellular infiltration.

"Sections from the wall of the larger ulcer also show a partial boundary of gastric mucosa. In areas the tubules at about their midpoint gradually merge into a structureless mass of rounded or polygonal cells which extend to, partly replace, and continue beyond the muscularis mucosæ as the remainder of the section. There is in many areas no definite stroma, in this mass of cells forming the newgrowth, connective tissue being very scanty. At each boundary of this area of transition of mucosa into the tumor, the latter extends below the muscularis without involving the overlying mucosa, the contrast between the structure of the two being very striking.

"Diagnosis: Both ulcers show carcinoma, which in each is in direct relation with the gastric mucosa. The structure of each, as above described, appears to justify the diagnosis of adenocarcinoma of the smaller ulcer and medullary carcinoma of the larger. In addition there is anatomical perforation of the larger ulcer, the opening being blocked by a mass of adherent newgrowth, presumably in a perigastric lymph node."

Dr. Despard and I have searched the literature dealing with multiple malignant growths, and one of the best accounts that we have been able to find is in Fenwick's[1] work.

Fenwick studied 1850 cases of cancer of the stomach, and in 54 or 2.9 per cent. multiple tumors were found, in three-fifths of these 54 cases, however, the tumors occupied corresponding spots on the anterior and posterior walls, and one showed a later development of the same type of cancer as the other. These were, in all likelihood, instances of transference by contact. Thus in about 1

[1] Cancer and Tumors of the Stomach.

per cent. there was no possibility of multiplication by contact, but in a number of these cases the growths were of exactly the same

FIG. 2.—Photomicrograph of section of smaller growth.

FIG. 3.—Photomicrograph of section of larger growth.

type and consequently can hardly be described as instances of multiple primary cancer of the stomach, a rare condition.

One of Fenwick's own cases presented a soft spheroidal-cell cancer of the cardia and a cylindrical-cell cancer of the pylorus. Several similar cases have also been collected from the literature by Fenwick.

D. D. Stewart,[2] reports a case operated upon by Dr. W. W. Keen, in which there were two isolated carcinomatous ulcers of the stomach: one was astride the lesser curvature of the stomach, and the other astride the greater curvature. The stomach in this case was removed post mortem, and a photograph of the specimen accompanies the report. Dr. A. O. J. Kelly examined the specimen and diagnosticated the condition as adenocarcinoma.

In Osler and McCrae's work on *Carcinoma of the Stomach* a case is reported of multiple submucous carcinoma of the stomach found at autopsy. The largest of the growths in this case was polypoid in character. The other growths were similar but smaller. From the histological character of the different growths Dr. Welch regarded the case as an instance of multiple primary carcinoma of the stomach.

Instances of multiple primary carcinoma occurring in different organs is more frequent than the occurrence of the condition in the same organ. Warthin[3] reports 2 cases of multiple cancer found post mortem. In the first there was an adenocarcinoma of the ovary and a colloid carcinoma of the gall-bladder. In the second case there was an adenocarcinoma of the sigmoid and an adenocarcinoma of the gall-bladder, each growth having started in a polyp and being of different anatomical character. In both of these cases stones were present in the gall-bladder.

Fenwick reports a case of spheroidal-cell carcinoma of the pylorus and a cylindrical-cell epithelioma of the rectum.

Albert Bauer, in an interesting inaugural address (Kiel, 1907) discusses at length the question of multiple primary carcinoma, and reports 3 personal cases. The first is that of "adenoma malignum" of the greater curvature of the stomach and "adenocarcinoma" of the pylorus, with glandular metastases from the latter. The second case showed an epithelioma of the esophagus, near the bifurcation of the trachea, and an adenocarcinoma of the stomach. The third case was one of squamous-cell epithelioma of the penis and adenocarcinoma of the stomach.

When two cancers of the same structure are found in the same organ the occurrence may usually be attributed to transference by contact or to autoinfection. It may be that the latter explanation would apply to my own case. The clinical history does not

[2] Amer. Jour. Med. Sci., November, 1898.
[3] Jour. Amer. Med. Assoc., May 6, 1899.

bear out the fact that we have a malignant change taking place simultaneously in two ulcers of the stomach. The patient was an intelligent man, and told me repeatedly that he never had any gastric symptoms until six or seven moths before his operaiton.

THE EFFECTS OF MEDICINAL DOSES OF ACONITE UPON THE PULSE RATE.

By R. D. Rudolf, M.D., (Edin.), F.R.C.P.,
PROFESSOR OF THERAPEUTICS IN THE UNIVERSITY OF TORONTO,
AND
C. E. C. Cole, B.A., M.B., (Tor.),
DEMONSTRATOR IN THERAPEUTICS IN THE UNIVERSITY OF TORONTO, CANADA.

The use of aconite as a medicine seems to date from 1762, when Baron Störck introduced the drug to practice. But aconite has been used by the laity from time immemorial, and few drugs have had a more varied history. Störck recommended the preparation as a diaphoretic and diuretic, and employed it in chronic rheumatism, gout, paralysis, phthisis, and a great variety of diseases. It was eagerly taken up by the profession, and for some years was enormously used, and then fell into disuse. In 1796 Hahnemann experimented with it, and recommended it in inflammatory fevers, where the allopathics would bleed. In 1835 M. Lombard, of Geneva, advocated its use as an anodyne and antiphlogistic in acute rheumatism and other acute local inflammations. "Under doses varying from ½ grain to 8 grains every two, four, or six hours the severest attacks of febrile rheumatism yielded in the course of two, four, or six days; and even protracted cases of subacute rheumatism were often cured. The relief of pain and abatement of fever commenced in a few hours, without any critical evacuation by the bowels, skin, or kidneys" (Christison[1]).

It appears to have been Alexander Fleming who first drew attention to the action of the drug in slowing the heart's beats. In 1845 he wrote a thesis upon the drug and showed how it slowed the heart's action. He described four stages, according to the amount given. After 5 minims of the tincture the heart slowed; the pulse, some four hours after the administration, would have fallen some eight beats. If a second dose were then given, or 10 drops had been given at first, the pulse would fall another eight beats and become weaker, but still regular. If two hours later 5 drops were again given the pulse would fall to perhaps half of its normal rate, but

[1] Dispensatory, 1848, p. 56.

still remain regular. In the fourth degree, after the taking of another dose of 5 drops, the pulse would become weak and irregular, and if the action of the drug were carried to a fatal extent the pulse would become gradually imperceptible. These results seem to be remarkable until we realize that Fleming used a tincture which was some six times as strong as the U. S. P. tincture, and therefore about twelve times the strength of the B. P. tincture. He made it by passing 24 fluidounces of rectified spirit through 16 ounces of powdered aconite root, while the U. S. P. tincture is 1 in 10 and the B. P. tincture about 1 in 20. Thus Fleming used doses corresponding to ½ to 1 dram of the U. S. P. tincture, the maximum official dose of which is 15 minims, and for repeated doses 1 to 5 minims.

Ringer and Murrell next introduced the employment of small but frequently repeated doses, and under the influence of the former's book, passing through its many editions, this method of using the drug has become widespread, although of late years one does not hear so much of it. Ringer especially recommended its use in the treatment of inflammations accompanied by fever, and indeed said: "In the treatment of inflammations the thermometer and aconite should go hand in hand."[2] He gave ½ to 1 drop (of the B. P. tincture) every ten minutes for two hours and then every hour, and such is the usual suggestion that echoes through most of the text-books to the present day. Under such treatment the pulse is believed to become slow, the fever to lessen, and the skin to become moist.

But in the doses recommended in the pharmacopœias, and still less in those suggested by Ringer and Murrell, the pulse does not seem, according to our observations, to be at all affected. With any other effects of the drug we are not here concerned.

One fact that stands out with great clearness is that aconite in sufficient amounts is a violent poison, acting powerfully upon the circulation, and finally killing by paralyzing the respiratory centre. Thus we found that 1 c.c. of a solution of the crystalline aconitine of 0.0225 per cent. (the strength of the B. P. tincture) killed a guinea-pig in a few minutes. In less powerful but still large doses it has a marked action on the heart, slowing it, chiefly through the vagus. S. A. Matthews[3] has recently shown how aconitine slows the heart of the dog and lowers the blood pressure. But he used $\frac{1}{16}$ mg. of aconitine (Boehringer's) injected and repeated in twenty minutes, which is an enormous dose. He concludes that the action consists in "a stimulation of the inhibitory mechanism of the heart, especially of the centres in the medulla. Next an increase in the irritability of the muscle of the auricle and ventricle." He says that "the first of these is the only effect seen in the therapeutic use of

[2] Handbook of Therapeutics, p. 343.

[3] Jour. Exper. Med., September, 1897.

the drug, and aconitine may, therefore, be considered to be indicated when it is desirable to stimulate the inhibitory centre without action on the heart muscle." This, of course, refers to very large doses, but, as already said, in doses such as are recommended in the pharmacopœias, and especially in the fractional doses introduced by Ringer and Murrell, the effect upon the circulation is *nil* according to our findings. These negative results may have been due to either of two causes: (1) Either the tincture used in the experiments was weak or inert, or (2) the doses were too small to have any appreciable effect.

F. W. Price found that several, in fact all, of the samples that he obtained from reputable druggists in England were inert when tested in Professor Cushny's laboratory. Next he obtained an active *aconitine* from this laboratory, and still found that the drug, even in doses far larger than those recommended in the British Pharmacopœia, had no effect upon the pulse rate, and, rather as a side issue, had no influence upon the blood pressure. These results were embodied in a paper which he presented before the Royal Society of Medicine in 1911.[4] During the past year the writers have tested the drug in many cases, as regards the effects upon the pulse rate, always using medicinal doses, and this paper gives the results of their work.

To commence with, we used the ordinary B. P. tincture, which happened to be in the Toronto General Hospital, and which had been obtained, as we afterward found, from three reputable firms of wholesale druggists. The pulse rate was usually taken for hours before and for hours after the administration, and in many cases the blood pressure was also measured, but no effect upon the circulation was detected. Often considerable fluctuations were seen, but it was found that these were mere coincidences and were just as apt to occur without the aconite. After finding no effects from the administration of the hospital tinctures we wrote to a well-known drug firm and they kindly forwarded a quantity of B. P. tincture "which has been tested both physiologically and by assay in the laboratory, and which we guarantee is of B. P. strength." Most of our experiments were done with this tincture, and were still negative. Then we asked Dr. V. E. Henderson, associate professor in charge of the pharmacological department of the University of Toronto, to test this tincture, and he reported it as very weak. The bottle had stood in a room at about 60° F. for some three months before he tested it, and probably had depreciated since we first obtained it, but our experiments were chiefly done soon after we got it. Next the same firm kindly sent us some pure crystalline aconitine, which Dr. Sharpe, of the pharmacological department, found by experiments on animals to be of full activity.

[4] Proc. Royal Soc. Med., June, 1911.

He was good enough to make for us a solution of it corresponding in strength to the B. P. tincture, namely 0.0225 per cent. (1 c.c. of this solution killed a guinea-pig in a few minutes), and we continued our experiments with this solution, still with negative results.

Our experiments were done upon two classes of patients: (1) Those with normal pulses, and (2) those with fast pulses. Some of the latter had fever and some had normal temperatures. In none of them (55 in all) was any decided effect upon the pulse rate observed. Occasionally the pulse would be found to be slow after the taking of the drug, but when the pulse was watched for hours before and after the administration it was seen that such fluctuations occurred without any aconite. The psychic effect of the administration, with the frequent taking of the pulse, must be taken into account. In one case of persistent tachycardia, following typhoid fever, the pulse dropped some forty beats for twelve hours after small repeated doses were given, which looked like a marked effect; but when the experiment was repeated upon the same individual under exactly the same conditions no such result, or rather sequence, occurred.

It appears from both Dr. Price's findings and our own that the tincture of aconite on the market is usually inert. We have discussed this matter with Dr. McGill, chief analyst to the Inland Revenue Department of Canada, and he hopes soon to examine samples from various parts of the Dominion, and the results will be interesting. The difficulties of testing the drug, however, are great. The aconite root contains at least three active principles—*aconitine, aconine,* and *benzaconine*—and, although it is an easy matter to assay the total alkaloids, it is very difficult to find the proportion of aconitine, and yet it is upon this alkaloid that nearly the entire action of the root depends. A simpler test, and one which is chiefly employed by the manufacturing houses, is the "Squibb test." This depends upon the fact that aconitine, and it only, produces, when applied to the tongue in great dilution, a tingling there. A solution of 1 in 500,000 of aconitine will give this reaction. Similarly a solution of 1 in 70 of the American tincture or 1 in 35 of the B. P. preparation should act in the same way. A dram of the dilution is held in the anterior part of the mouth for exactly one minute and is then discharged. A distinct tingling should be perceived within ten to fifteen minutes. Mr. F. O. Taylor,[5] who has written extensively upon the tests for aconite, and gives a very complete bibliography, believes that this is the best practical test that we possess. None of the tinctures that we procured gave this reaction, but the solution of crystalline aconitine which was of the strength that the tincture should be, and was then diluted as described, gave it very distinctly. It is interesting, however,

[5] Jour. Industrial and Engineering Chemistry, August, 1909.

to note that this same solution would not give the Squibb test three months later until diluted four times less than before, which shows how aconite depreciates with keeping.

Even when the drug is active, small doses seem to have no effect upon the pulse rate. How then may we explain the reports to the opposite effect which teem in medical literature, and which support the advice found in nearly every text-book on therapeutics and medicine. To our minds it is another example of the *post ergo propter* fallacy, which fallacy is so often seen in medicine, and which has so frequently been responsible for many findings which further trial has shown to be without foundation—something is given and the patient improves: *ergo*, the improvement is due to the something given.

The examples of marked and even dangerous effects following small medicinal doses of aconite, which are occasionally chronicled, can only be due to one of two things: (1) Either there has been some mistake in the dispensing or administration of the drug, so that the patient has received far more than was intended, or (2) an idiosyncrasy must have existed so that toxic effects were obtained from a dose which ordinarily has no effect. For example, Woodbury[6] records a case of nearly fatal poisoning from 3 drops of the tincture. No doubt, as Shoemaker[7] says, "The toxic dose and the susceptibility to aconite both vary greatly in different subjects."

It can truly be said that the theme of this paper is destructive rather than constructive, but surely the subject of therapeutics almost more than any other part of the domain of medicine requires destructive criticism in order that we may clear away the chaff and thus make more clear the valuable parts that remain. The pharmacopœias of old contained many weird substances, such as human urine, which were gravely prescribed by earnest men, and good followed; and yet we do not believe nowadays that that good resulted from the remedy used. And the pharmacopœias of today contain many substances which might well be left out, and we believe that aconite, certainly in the doses recommended, is one of these.

As already said, aconite, when given in massive doses, is an extremely powerful body, and it may be of great value where it is desired to slow the pulse or obtain some of its other effects; but this paper is not dealing with such uses of the drug at all.

[6] Proc. Coll. of Phys. of Philadelphia, 3d series, x, 450.
[7] Mat. Medica and Therap., p. 151.

Dosage of B. P. tincture.	Condition of patients.	Age.	Effects on pulse rate.
One minim every ten or fifteen minutes for eight to ten doses.	Eight convalescents with normal pulse rates.	..	Nil.
	Eight convalescents with fast pulses.	..	Nil.
	Post-typhoid tachycardia.	25	Nil.
	Post-typhoid neuritis.	45	Nil.
	Two healthy orderlies.	..	Nil.
	Tuberculous knee.	20	Nil.
	Typhoid fever.	22	Nil.
Two minims every ten to fifteen minutes for eight to ten doses.	Acute tonsillitis.	23	Nil.
	Hysterical vomiting.	21	Nil.
	Cholecystitis.	50	Nil.
Three minims every ten to fifteen minutes for eight to ten doses.	Convalescent typhoid.	25	Nil.
	Gallstones.	28	Nil.
	Rheumatoid arthritis.	23	Nil.
	Streptococcic septicemia.	24	Nil.
	Pleuropneumonia.	55	Nil.
	Septicemia.	24	Nil.
Four minims every ten minutes for eight doses.	Convalescent pleurisy.	28	Nil.
	Pleuropneumonia.	25	Nil.
	Pleuropneumonia, repeated.	..	Nil.
Four and one-half minims every ten to fifteen minutes for eight to ten doses.	Phthisis pulmonalis.	30	Nil.
	Convalescent typhoid.	25	Nil.
	Rheumatic arthritis.	60	Nil.
	Hysteria.	22	Nil.
Two minims every hour for four doses.	Convalescent typhoid.	25	Nil.
Three minims every hour for ten doses.	Convalescent typhoid.	25	Nil.
	Tuberculosis.	30	Nil.
	Mitral stenosis.	22	Nil.
	Gallstones.	22	Nil.
	Arthritis deformans.	21	Nil.
Four and one-half minims every thirty minutes for ten doses.	Tuberculosis.	30	Nil.
Six minims every hour for ten doses.	Post-typhoid neuritis.	45	Nil.
	Arthritis deformans.	22	Nil.
Ten minims every hour for ten doses.	Exophthalmic goitre.	18	Nil.
	Splenomyelogenous leukemia.	45	Nil.
	Chronic rheumatism.	25	Nil.
One dose of fifteen minims.	Neurasthenia.	21	Nil.
	Rheumatoid arthritis.	25	Nil.

LUPUS ERYTHEMATOSUS AND RAYNAUD'S DISEASE.

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M. C., a young unmarried woman, aged twenty-four years, first came under observation at the Skin Dispensary of the University Hospital, Philadelphia, in December, 1908, where she

had come for advice concerning a disease of the skin affecting principally the hands and feet, more especially the fingers and toes. At this time the fingers, which were apparently somewhat atrophied, were a deep bluish-red color with a number of small pearly white, stippled, scar-like patches scattered over their palmar surface, and a small, thickly crusted ulcer on the palmar surface of the second phalanx of the left thumb, and one on the tip of the left index finger. The palms were also affected, but to a much less degree than the fingers, showing only two or three small scar-like areas in each, and a single small oval ulcer on the ulnar side of the left one. The toes of both feet were quite livid, the discoloration being patchy on the smaller ones, and there were a considerable number of small scar-like lesions like those on the fingers. In addition to these lesions on the fingers and toes there was a very ill-defined, rather dusky patch on the right ear. Tactile sensation in the fingers was somewhat impaired, and the patient occasionally complained of a numb feeling in the hands as if, to quote her own words, "a rubber band was around the wrist." She suffered much from a most distressing burning and aching of the fingers and toes which was not continuous, but came on at irregular intervals, being especially severe just preceding the formation of the ulcers. The disease had lasted two years and had finally compelled the patient to give up her occupation, which was that of a saleswoman.

During the next few months there was but little change in the condition of the fingers. It was noted that the lividity varied much from time to time and was apt to occur paroxysmally; on one occasion the patient stated that while on her way to the dispensary the right ring-finger became "quite black" for a short time. It was noted, too, that the tips of one or more of the fingers became dead-white and waxy looking at times and remained so for a period varying from a few hours to two or three days, this condition being occasionally followed by the appearance of small blebs in the same situation and later by superficial eschars. Small ulcers similar to those upon the fingers occurred upon the toes, but apparently less frequently.

In May, 1909, a small, oval, violaceous, slightly scaly patch was observed on each upper lid near the inner canthus, which presented the features of an ordinary lupus erythematosus, these with the faint patch on the ear already referred to being the only evidence of cutaneous disease noted elsewhere than upon the extremities throughout the entire period of observation. During the summer months of this year the condition of the hands was somewhat improved; they were less discolored and there was much less pain, except for a period of a week or two in June when there was a rather severe inflammation with suppuration about the roots of the nails. With the advent of colder weather, however,

about the end of October, the fingers became much redder, there was a decided increase in pain, and a considerable number of small flaccid blebs appeared upon the hands, palms as well as fingers. According to the statement of the patient there was always a marked increase in all the symptoms with the appearance of cold weather, but this was the severest attack she had ever had. Throughout the winter of 1909–1910 small pea-sized ulcers continued to appear at irregular intervals upon the hands and toes, usually preceded by small blebs, the patient complaining much of pain while these were forming. About the end of March, 1910, she ceased attendance at the dispensary, but it was learned subsequently from a sister that the condition of the hands remained much the same during the next year. She then had a severe attack of facial erysipelas complicated by malignant endocarditis which terminated fatally.

To recapitulate the salient features of this unusual case, there were (1) certain vascular phenomena, such as cyanosis of the extremities alternating with extreme local ischemia frequently followed by the formation of blebs and superficial necrosis of the ischemic areas, accompanied by severe burning and aching, aggravated by cold, symptoms characteristic of Raynaud's disease; and (2) violaceous patches on the ear, eyelids, and toes, with numerous small, bluish-white, atrophic areas on the hands and feet, lesions characteristic of erythematous lupus.

The association of erythematous lupus with certain vascular symptoms, such as cyanosis of the hands and feet, the ears, and nose, especially noticeable in cold weather has frequently been noted by dermatologists, and special names have been employed to designate the forms of the disease in which such symptoms are a prominent feature. Practically no mention, however, is made in text-books on diseases of the skin of cases presenting the very marked vasomotor symptoms described in some detail in the case just reported, although I have found an unexpected and relatively considerable number of cases resembling it more or less closely, scattered throughout the journals devoted to dermatology. A brief review of the cases which I have collected will not only serve to illustrate the character of the relationship between these two maladies, but will demonstrate, as I believe, that the relationship is intimate and real and not accidental.

CASE I.—A woman, aged thirty-five years, who suffered from a joint affection which was regarded as chronic rheumatism, had numerous small ulcerations on the face, forearms, and feet which left conspicuous white scars. The skin of the face was stiff and wooden, like morphea. The fingers became white and cold, and subsequently dusky, upon the slightest exposure, and many of the nails became inflamed and suppurated at their roots. Upon the abdomen and over the front of both thighs were erythematous

patches presenting the characteristics of erythematous lupus. The case was regarded by Mr. Hutchinson,[1] who reported it, as a mixed one of erythematous lupus and Raynaud's disease.

CASE II.—An unmarried woman, aged nineteen years, was the subject of a peculiar vesicating erythema of both cheeks, which was looked upon by Mr. Hutchinson[2] as most likely an irregular form of lupus erythematosus. In addition to this affection of the cheeks the fingers were swollen, dusky, and cold, with deep-seated vesicles along the sides; the ears were swollen in like manner, and the nose was cyanotic and cold. Puffy swellings developed on the extremities in the course of a few hours, then rapidly disappeared, leaving greenish-yellow, bruise-like stains.

CASE III.—A woman, aged twenty-three years, had at first "typical Raynaud's disease," resulting in gangrene of the tips of some of the fingers, and this was followed one year later by a "bat's wing" erythematous lupus of the face. Two years later the hands presented a characteristic sclerodactylia, and there was likewise a sclerodermia of the face (Pringle).[3]

CASE IV.—A delicate girl, aged seventeen years, had an accurately symmetrical "bat's wing" patch on the face containing numerous dilated sebaceous-gland ducts. The hands were blue and cold, and were covered with livid erythematous patches, as also were the toes. The tips of both little fingers were gangrenous, while gangrene of several others seemed to be impending; the disease was accompanied by great pain. The case was shown as one of lupus erythematosus and Raynaud's disease.[4]

CASE V.—A neurotic woman, aged forty-four years, had attacks of localized syncope alternating with local asphyxia of the extremities, particularly of the hands. The nutrition of the fingers was much impaired; they were stumpy and atrophied, but gangrene had not occurred. Five years later erythematous lupus occurred in the temporal region and on the scalp. This patient suffered much from cold.[5]

CASE VI.—A single woman, aged twenty years, had a scaly eruption occupying the ears, cheeks, nose, and backs of the hands, of seven years' duration, which was regarded as an erythematous lupus. In addition to this eruption the tips of both little fingers were much atrophied, and the patient complained of the fingers "going dead" in cold weather (Cavafy[6]).

CASE VII.—A woman, aged twenty-four years, suffered from daily attacks of asphyxia of the hands, which became black and numb. In addition to these symptoms the patient had acne necrotica of the hands and forearms and an erythematous lupus of the scalp (MacKenzie[7]).

[1] Arch. Surg., i, 22.
[2] Ibid., iii, 122.
[3] British Jour. Derm., vi, 339.
[4] Ibid., vii, 30.
[5] Ibid., xvii, 143.
[6] British Jour. Derm., ix, 328.
[7] British Jour. Derm., x, 10.

CASE VIII.—A woman, aged thirty-four years, who presented unmistakable symptoms of Raynaud's disease, such as alternate pallor and cyanosis of the extremities, had likewise lesions characteristic of erythematous lupus upon the backs of the hands and fingers (Little[8]).

CASE IX.—A woman, aged twenty-six years, had an extensive atrophying erythema of the face, nose, cheeks, and external ears; there were large areas of ivory-white skin dotted over with greatly dilated sebaceous-gland ducts. The scalp was also involved. The hands and feet were always very cold, the fingers much wasted, with impending gangrene of the finger tips. Warde[9] regarded the case as one of atrophic Raynaud's disease associated with erythematous lupus. This same author[10] noted the presence of so-called "dead fingers" in 3 out of a series of 15 cases previously published.

CASE X.—A woman, aged twenty-four years, had suffered from erythematous lupus for twenty years, the disease first appearing on the tip of the nose, spreading thence slowly to the cheeks. Some time later the fingers became affected, and progressive wasting followed. The hands were alternately either "very cold or very hot." The case was exhibited by Sequeira[11] as one of erythematous lupus accompanied by a condition of the fingers "simulating Raynaud's disease."

CASE XI.—A man, aged forty-nine years, had characteristic patches of erythematous lupus on the face, ears, scalp, back of the hands, and fingers. For some time he had complained of his fingers "going dead and white," and actual necrosis of the end of the little finger and lower part of the helix of the right ear had taken place. There were also small eschars on the back of the fingers and on the nose which left slight scars.[12]

CASE XII.—A man, aged sixty-eight years, who had an eruption on the cheeks, ears, and scalp, consisting of red, scaly patches containing atrophic areas, lost several toes by gangrene which had followed an asphyctic condition. The reporters, Engman and Mook,[13] regarded the case as erythematous lupus and Raynaud's disease.

CASE XIII.—A woman, aged thirty years, who in 1894 had been shown at a meeting of the Société Française de Dermatologie et de Syphiligraphie as a case of sclerodermia, six years later developed local asphyxia of the extremities and gangrene with partial destruction of the terminal phalanges, and erythematous lupus. (Hallopeau and Trastour[14]).

In one of the cases reported by Mr. Hutchinson and in my own, suppuration at the roots of the nails occurred at one stage of the

[8] British Jour. Derm., xvii, 104.
[9] Ibid., xv, 279.
[10] Ibid., xiv.
[11] Ibid., xix, 427.
[12] Ibid., xxiii, 182.
[13] Interstate Med. Jour., April, 1909.
[14] Annales de Dermatologie et de Syphiligraphie, 1900, Tome I, 4ième série, p. 634.

disease, a most unusual symptom more likely to have been the result of the vascular disturbances than a part of the erythematous lupus.

In 4 of the cases the symptoms of the lupus followed the vascular disturbances; in the remainder the sequence of the symptoms is not stated. In 1 case (Case V) not less than five years elapsed between the beginning of Raynaud's disease and the appearance of the erythematous lupus.

In some of the discussions which followed the presentation of these cases (nearly all of them were exhibited before English or French dermatological societies) it was objected that the vascular symptoms were not indicative of true Raynaud's disease, chiefly because they were more or less continuous. I do not believe this objection to be well founded, however, since in 6 out of the 14 cases here considered (including my own), nearly 43 per cent., the vascular symptoms were more or less distinctly paroxysmal. Indeed, those cases in which extreme local ischemia was followed by the formation of bullæ and superficial gangrene of the skin of the fingers and toes seem to me to have been typical cases of Raynaud's disease. In the case reported by Engman and Mook, however, it is somewhat doubtful, as the authors themselves admit, whether the gangrene was of the Raynaud type; it seems rather to have been the result of senile changes in the arteries.

The circulatory symptoms very briefly described in the cases which I have here reviewed leave very little room for doubt that in most if not all of them the erythematous lupus was associated with actual Raynaud's disease, or at least, with an affection which simulated that malady so closely as to be practically indistinguishable from it.

The nature of the relationship existing between these two maladies must, for the present at least, remain largely a matter of conjecture; we know too little about their pathogenesis to satisfactorily explain their occasional coexistence. I believe the relationship which undoubtedly exists between them may be best explained by supposing both at times to be due to a common cause, most probably some toxin circulating in the blood, which acts primarily upon the vessel walls producing vasomotor and inflammatory changes in the skin and subcutaneous tissues. Indeed, cases of the kind here considered seem to me to go far in support of the view that erythematous lupus should be regarded as a toxic erythema.

SOME FEATURES OF THE GROSS ANATOMY OF THE SPINAL CORD AND NERVE ROOTS, AND THEIR BEARING ON THE SYMPTOMATOLOGY AND SURGICAL TREATMENT OF SPINAL DISEASE.[1]

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During the last year I have made a number of dissections of the human spinal cord, nerve roots, and membranes in order to study their arrangement and relations. Some of the observations made are recorded in what follows.[2]

The Structure of the Posterior Roots as the Explanation for the Peculiarity of Root Symptoms at Different Levels. As is well known, the anterior and posterior nerve roots perforate the dural sheath separately, with a thin septum of dura mater between them. In the cervical region (Fig. 1, *A*) the nerve bundles of the posterior roots remain distinct until they have passed through the dura. The bundles are spread out like a fan, the broadest part being at the cord. At their origin the bundles are spread out so as to occupy 1 to 2 cm. of the cord; between their origin and the dura they lie closer together, forming a layer 1 to 1½ cm. broad; at the dural openings the nerve bundles are still distinct. In the dorsal and lumbar regions the arrangement is different from that just described; the separate bundles soon combine to form one bundle (Fig. 1, *B*), which passes outward to the dural opening as the posterior root.

From this arrangement it is clear that in the cervical region a tumor will, for a long time, make pressure only upon a few of the bundles which go to make up a posterior root. In the dorsal and lumbar regions the nerve bundles are united into one nerve near the cord; a tumor in these regions will press upon the whole nerve root from the beginning. Clinical experience agrees with these anatomical facts: the earliest symptoms of pressure upon a cervical nerve root are usually confined to a small area of distribution, one or two fingers for example, while in the dorsal or lumbar region the classical root symptoms extend over entire root areas. It is more exact therefore to distinguish between "root bundle" and "root" symptoms, and this distinction should be of clinical value.

The Intradural and Extradural Course of the Posterior Roots and its Significance. A careful dissection of the posterior roots of the

[1] Read at the October (1912) meeting of the New York Neurological Society.

[2] The dissections were done in the anatomical laboratory of the Fordham University Medical School.

spinal cord will show that there are very marked differences in their course at different levels. In the cervical and upper dorsal regions the nerve bundles unite to form the posterior root and pass out of the dural sac at almost a right angle to the cord. They then perforate the dura and enter the posterior ganglion (Fig. 2, *A*). From the ganglion each root passes outward with a slight inclination upward.

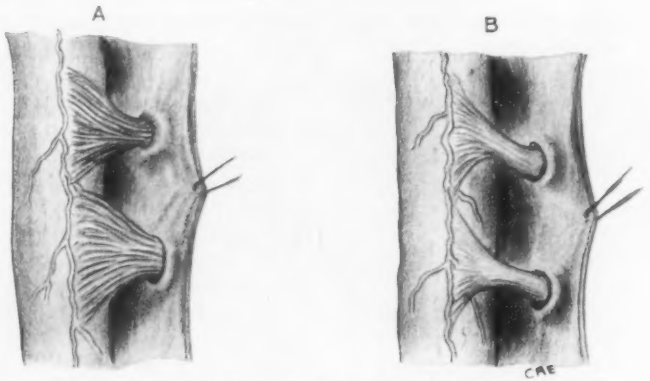

FIG. 1.—*A*, two cervical posterior roots; *B*, two dorsal posterior roots.

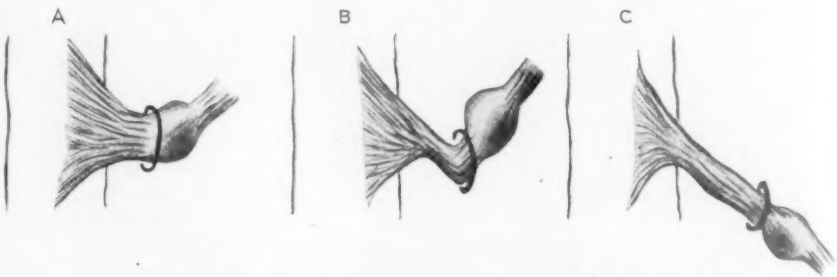

FIG. 2.—The course of the posterior spinal roots. *A*, cervical; *B*, dorsal; *C*, lumbar. Note the marked angle of the dorsal root just before it perforates the dura.

From the eighth cervical to the middorsal region the course of the posterior roots is different. Each root has an inclination downward until it nears the dura; it bends upward at an angle just as it perforates the dura. In the middorsal region this angle is often very acute—40° to 45° (Fig. 2, *B*). Beyond the ganglion each posterior root passes markedly upward before it divides into its anterior and posterior branches.

In the lower dorsal and lumbar regions the posterior nerve roots pass downward and outward and perforate the dura; beyond

the ganglia the direction remains unchanged until the nerve roots divide into their anterior and posterior branches (Fig. 2, *C*).

It is easy to understand, when one considers the striking angle in the posterior roots in the dorsal region, that only a slight inflammatory process near the dural opening may be responsible for the occurrence of marked root symptoms.

It is probable that the movements of the vertebral column (bending backward and forward) will increase an existing pressure upon any of the lower dorsal and lumbar posterior roots, because these cannot yield as easily as the upper dorsal roots. Root symptoms in the lower dorsal and upper lumbar regions should become much intensified with forward and backward movements of the vertebral column. To a less degree this must also be the case in the cervical region, although here the bundles of the posterior roots are spread over such a large area that all are seldom pressed upon at the same time. Lateral movements of the spine are apt to increase a root pain on the opposite side and to lessen a root pain on the same side to which the spine is bent. These facts probably have an important bearing upon the occurrence of rigidity of the spine, which is found in patients who have a tumor in the lower dorsal and upper lumbar and also in the cervical cord.

The Relation of the Ligamentum Denticulatum to the First Lumbar Root and the Surgical Importance of this Relation. The ligamentum denticulatum is a fibrous band which is derived from and attached to the lateral aspect of the pia mater on the cord midway between the anterior and posterior roots. On each side of the cord the ligament extends from the foramen magnum to the level of the first lumbar vertebra. From its attachment to the cord each ligament extends outward and is attached to the inner surface of the dura by numerous dentations or slips. This ligament divides the subarachnoid space into an anterior and posterior compartment. It is due to this ligament that a tumor which grows on the anterolateral or posterolateral aspect of the cord will press upon only anterior or posterior roots for a long time, and thus give only anterior or posterior root symptoms before the appearance of symptoms of pressure upon the cord itself.

The dentate ligament ends below, at the level of the first lumbar vertebra, in a fork-shaped extremity (Fig. 3, *L*, *D*). The outer prong of the fork is usually about 1 cm. long, and is attached by its end to the inner surface of the dura. Sometimes this prong is 3 or 4 cm. long. The inner prong of the fork is attached to the pia on the lateral aspect of the cord and is prolonged downward along the side of the conus to its tip.[3] The first lumbar posterior

[3] The filum terminale is described in the text-books as derived from the pia mater of the cord. It is really the prolongation downward of the inner prong of the fork of the dentate ligament, and is formed by the fusion of the downward prolongations of the ligaments of the two sides.

root rests upon this fork (Fig. 3), so that the "fork" may be used as an anatomical landmark for the identification of the first lumbar root. The posterior roots of the lumbar and sacral nerves are dorsally placed with reference to the fibrous band on the side of the lumbosacral cord and conus derived from the dentate ligament, and can be easily raised up with a probe which is bent to a slight curve. At their origin from the lumbosacral cord the posterior roots lie close together, but when they are raised up with the probe the separate roots can be recognized. If one begins to count from the posterior root which lies on the fork of the dentate ligament, which is the first lumbar, one can easily identify each posterior root.

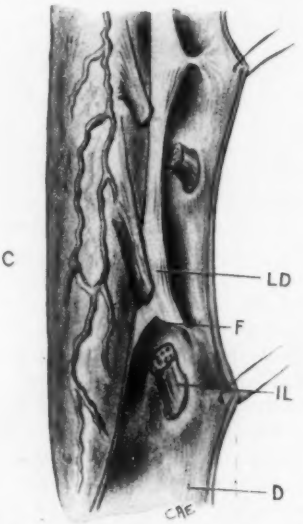

FIG. 3.—The lower end of the ligamentum denticulatum. *LD*, showing the "fork," *F*; *C*, conus; *D*, dura laid open; *IL*, first posterior lumbar root. The root has been divided to show the fork of the dentate ligament.

The importance of these anatomical facts for the operation of division of posterior roots to the lower extremities is clear. In this operation it is usually necessary to divide four or five posterior roots on one or both sides, and, therefore, four or five laminæ have to be removed so that the roots can be identified at the points where they perforate the dural sac. Sometimes it is not easy or certain that one has separated the posterior from the anterior root. To avoid this extensive laminectomy, van Gehuchten, Codivilla, and Wilms and Kolb have suggested that the nerves should be exposed at their origin from the lumbosacral cord by the

removal of three laminæ in the dorsolumbar region. According to these authors, however, it is difficult to recognize the roots to be cut, and there is danger of division of the anterior roots with the posterior ones.

Based upon the anatomical facts above described, I have, in the cadaver, exposed the lumbosacral cord by the removal of the laminæ of the eleventh and twelfth dorsal or eleventh and twelfth dorsal and first lumbar vertebræ, and have been able to recognize and divide the lumbar and sacral posterior roots desired. I desire to recommend the following method for the exposure and division of posterior roots to the lower extremities: Removal of the spinous processes and laminæ of the eleventh and twelfth dorsal vertebræ (and of the first lumbar if necessary) in the usual manner; exposure of the "fork" of the dentate ligament and identification of the first lumbar posterior root; careful elevation of all of the posterior roots of the side to be operated upon (which lie dorsal to the lateral fibrous band on the side of the lumbosacral cord) upon a bent probe passed under them; identification and isolation of the desired posterior roots by counting from the first lumbar root; division of the roots in the usual manner.

BENCE-JONES PROTEINURIA: A REPORT OF FOUR CASES, WITH SOME CHEMICAL AND BIOLOGICAL NOTES.[1]

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I. Introduction. Having had the unusual opportunity of studying, with more or less completeness, 4 cases of Bence-Jones proteinuria, it seems to the writers worth while to record these briefly with some observations on the methods of recognition, chemical properties of the body, and certain biological reactions. The work of Magnus-Levy,[2] Grutterink and de Graaf,[3] Abderhalden and Rostoski,[4] and especially the recent exhaustive con-

[1] Read at the meeting of the Association of American Physicians, May 14, 1912.
[2] Zeit. f. phys. Chem., 1900, xxx, 200.
[3] Ibid., 1902, xxxiv, 393; ibid, 1905, xlvi, 472.
[4] Ibid., 1905, xlvi, 125.

tribution of Hopkins and Savory,[5] have made it certain that this body is not an albumose, but a true protein, yielding the characteristic amino-acids on hydrolysis. The theories as to its origin are quite numerous, but in the light of recent investigations the more important are those which seek its derivation (1) from the proteins of the tissues or blood, (2) specifically from the tissues of the bones, or (3) as a product of abnormal protein metabolism, either endogenous or exogenous. Of these the preponderance of evidence seems to favor the idea that the enormous output of the protein is rather due to the influence of the tumor, or its products, on the tissue metabolism, than the direct product of a relatively small amount of tumor substance present in the body. The great majority of the cases in which this body has been found in the urine have been instances of multiple myeloma, although not all individuals suffering from this disease have exhibited Bence-Jones proteinuria. In isolated instances it has been found associated with other pathological conditions, such as leukemia, chloroma, lymphosarcoma, myxedema, and carcinomatous metastases (1 case). It is also to be noted that some of the reported occurrences associated with leukemia and osteomalacia were subsequently found to be cases of multiple myeloma. The most complete historical review which has come to our notice is that of Rosenbloom.[6]

II. Case Reports. Case I.—C. F., white, female, aged fifty-four years. Patient of Prof. Gordon Wilson, Baltimore.

Complaint: Rheumatism. Family History: unimportant. Past History: intermittent fever at twenty. When aged twenty-six years fell and hurt left leg, which two years later broke down and ulcerated. Treated several years in the Johns Hopkins Hospital Dispensary. Normally well until October, 1909, when she began to have pains in left leg, which extended to her back and neck, and developed swellings, considered to be rheumatic, in feet and legs, which gradually involved the larger joints of the arms as well. In the winter of 1909 she began to have gastric disturbance, regurgitation of food, not much nausea, no hematemesis, and great wasting. Was considered to have carcinoma of the stomach. Became bedridden, owing to joint troubles and weakness. In May, 1909, she developed severe pains, worse at night, often lancinating in character, in both arms and legs. Gradual atrophy of muscles and stiffness. Severe diarrhea developed in summer of 1910, with abatement of gastric symptoms. Frequent small mucous stools, but no blood. At times incontinence of feces. In the fall and winter of 1910-11, increasing polyuria, with cystitis. Bence-Jones protein was found in the urine by Dr. Wilson in January 1911; it had not been observed in the last previous examination, October, 1910.

[5] Jour. Physiol., 1911, xliii, 189.

[6] (Exhaustive bibliography to 1911) Biochemical Bulletin, 1911, i, 161.

Patient was first seen by us January 20, 1911, at which time she showed great emaciation and rigidity of the extremities. Pupillary reactions normal. There was a moderate stomatitis, with some salivation (not due to mercury). Tongue very thick, pallid, with marked hypertrophy of the papillæ. Buccal mucous membrane opaque and soft. No abnormality in lungs. Heart slightly enlarged, and showed a well-compensated mitral stenosis and insufficiency. Peripheral arteries sclerotic. Pulse of good volume, regular, 80. Blood pressure: systolic, 110 to 120 mm. Hg. Abdomen scaphoid. No abnormal pulsation or peristalsis. No masses made out on palpation. Pelvic organs apparently normal. Extremities: marked thickening about large joints, with limitation of motion and pain on manipulation. No acute inflammatory changes. Terminal phalanges of fingers and toes somewhat enlarged and clubbed. Left tibia was distinctly enlarged throughout the greater part of the shaft, but not rough or irregular. No enlargement of ribs or bone tenderness there or elsewhere in skeleton made out. Rather marked diffuse keratosis in palms and plantar surfaces of feet. Patient was subject to occasional syncopal attacks, in which she apparently had a weak pulse, without convulsions. Marked cutaneous hyperesthesia on palms and soles of feet. At this time there was polydipsia and polyuria. Blood: rather marked secondary anemia. Normal white blood count and differential. Wassermann: negative.

Urine: Amount, twenty-four hours, 2350 c.c.; pale yellow; cloudy; faintly alkaline; specific gravity, 1014; heavy white sediment of granular debris; epithelial cells; no casts, blood, or pus; no sugar; biuret reaction positive; abundant carbonates; uric acid, 0.54 gram; total nitrogen, 12.68 gram; total chlorides, 2.3 gram. (During the last few months of life it was impossible to secure a twenty-four hour specimen, but total amount of urine was about 500 c.c. per day, giving a total chlorides of 3 grams). Polarization after removal of protein negative; diacetic acid and acetone absent; urobilin present; total protein, 2 grams to liter (Tsuchiya); Heller's nitric acid test gave a heavy white ring at contact line; with heat and acetic acid the protein precipitated between 56° C. and 60° C.; partial resolution on boiling and reprecipitation on cooling; filtrate gave no biuret or Adamkiwicz tests; with dilute nitric acid (25 per cent.) characteristic precipitation in the cold, with nearly complete solution on boiling and reprecipitation on cooling.

The case was observed at intervals until her death, May 6, 1912. The polyuria disappeared, partly owing to increasing stomatitis and difficulty in swallowing. Tongue became so large as to practically fill the mouth, deep red in color, marked superficial maceration. In December, 1911, patient was seen again after four months, when a nodule was noted on the anterior border

of the left scapula, hard and apparently continuous with the bone. This gradually increased, reaching the size of a hen's egg before death. In February, 1912, there was tenderness over the third and fourth ribs, left precordium, and axilla, but no nodules were made out. This persisted and increased, ribs becoming eventually definitely nodular, and six days before death they caved in. Coincident with this there developed a pericardial friction rub of great intensity with extreme pain. There was tenderness over most of the thoracic spine, but no nodes were discovered. In April, 1912, nodules were noted over the anterior surface of both elbows about the condyles; there was a brawny induration of the fingers, very like scleroderma, with an extraordinary overgrowth of the horny layers of the skin and a hypertrichosis of the hairs of the face. At this time there was noted a mass extending from the anterior superior spine of the ilium on the left side, half-way to the pubis, which was firm, elastic, and exquisitely sensitive. It caused great pain, referred to the distribution of the anterior crural nerve. A similar, but smaller, mass was felt just behind Poupart's ligament on the right side, near the pubis. These, with the nodules on the other bones, increased with great rapidity during the last four weeks of life, the one on the left ilium reaching the size of a large orange. The inguinal, axillary, and epitrochlear glands became enlarged during this period; they were discrete, firm, and sensitive to the touch. The patient lost all ability to swallow, apparently owing to the enormous swelling of the tongue. Articulation was much impaired. She took no food or water during the last week of life.

X-ray examination, made in February, 1912, with a portable apparatus was unsuccessful, with the exception of the plate of the left tibia, which showed an enlarged, swollen tibia. "There were no absolute areas of bone destruction, but there was a laminated rarefaction, extending throughout the tibia. From the *x*-ray examination it would be impossible to state definitely that this change was myeloma. In fact, the bone change simulates more closely the changes one sees in Paget's disease."

No autopsy was permitted.

During the entire period of observation (fifteen and one-half months) the urine showed constantly a reaction for Bence-Jones protein.

CASE II.—C. G., white, male, aged fifty-two years. Patient of Prof. H. G. Beck, of Baltimore, who kindly gave us his notes and a specimen of urine after the death of the patient, January 7, 1912.

Abstract of Dr. Beck's notes: "Patient was first seen September 8, 1911. Had been ailing for some months. Complained of shortness of breath, poor memory, weakness, and loss of weight. Physical examination showed arteriosclerosis, hypertrophied heart, aortic

and mitral regurgitation. Blood pressure, 215 mm. Hg. Urine gave a large precipitate with acetic acid and potassium ferrocyanide, but none by heat.

"September 15: Urine contained a large amount of albumose, but no serum albumin.

"October 17: Urine showed precipitate with acetic acid and potassium ferrocyanide, but none on boiling.

"December 2: An attack of acute paroxysmal pulmonary edema. Very cyanotic. Frothy, serous expectoration. These attacks have been noted several times in the last four years, occurring at night and lasting several hours.

"December 10: Urine showed (1) an opacity at 50° C., precipitate at 70° C., partial clearing on boiling; (2) complete precipitation with two volumes of saturated ammonium sulphate solution; (3) no precipitate in cold with acetic acid.

"December 18: Examination of chest shows small elevations on ribs almost nodular, but no tenderness. *X*-ray picture of chest does not show any bony changes.

"December 23: Differential leukocyte count normal. Hemoglobin, 58 per cent.

"January 7, 1912: Patient died suddenly after being out all day, apparently of acute dilatation. No autopsy was secured."

Specimen of urine submitted for our examination by Dr. Beck showed characteristic reaction for Bence-Jones protein; precipitation with heat and acetic acid between 54° C. and 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate yielded no test for protein. Typical reactions also were obtained with 25 per cent. nitric acid, and on addition of two volumes of saturated solution of ammonium sulphate. Urine: Clear; acid; specific gravity, 1013; no sugar; total protein, 1½ grams per liter (Tsuchiya); total chlorides, 5 grams per liter; no casts.

Case III.—S. S., white, male, aged sixty-four years. Patient of Dr. Henry M. Fitzhugh, Westminster, Md. Admitted to the Johns Hopkins Hospital, January 9, 1912, under the care of Prof. T. B. Futcher.

Complaint: Pain in the left lumbar region and at the navel. Family History: unimportant. Previous History: unimportant. Present Illness: began about two months ago, pain on left side under costal margin, worse in the afternoon and at night. Eructation, no vomiting, no blood in stools.

Examination: Large man, undernourished, slightly anemic. Pupils react normally. Thorax symmetrical. Lungs clear. Heart normal. Pulse normal, no marked peripheral sclerosis. Blood pressure, 180 mm. Hg. Abdomen: no abnormality other than palpable right kidney. Rather marked dermatographia. Exaggeration of deep reflexes. No general glandular enlargement. No enlargement or nodes noted over long bones or ribs. Tenderness

over eleventh and twelfth ribs, on left side. Patient thinks he may have injured this side some six months ago.

Ewald test meal showed marked hyperacidity.

Blood: Red blood cells, 3,800,000; leukocytes, 14,000; hemoglobin, 55 per cent. Differential count shows increase in polymorphonuclear neutrophiles.

"*X*-rays: Lumbar spine negative. Ribs show small vacuolated areas; similar areas in right humerus, due to bone destruction. These areas are sharply defined and there is slight new bone formation around the edge, showing an attempt to limit the disease."

Urine gave characteristic precipitation at 54° C., complete at 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate free from protein. Precipitate insoluble in water, but readily soluble on heating with dilute sodium carbonate solution, latter removed by dialysis, leaving the protein in solution. With 25 per cent. nitric acid there was precipitation in cold with an almost clear solution on boiling, reprecipitation on cooling.

During twenty days of the patient's stay in the hospital the total daily amounts of urine were examined. The Bence-Jones protein was constantly present, and was the only protein demonstrable. The total amount of urine varied between 2000 and 2800 c.c. Specific gravity, 1006 to 1010; total protein, 5 to 7 grams (Tsuchiya); total chlorides varied from $1\frac{1}{2}$ to $4\frac{1}{2}$ grams; coarsely and finely granular casts were found at each examination.

Patient lived about thirteen weeks after leaving the hospital, all the urine being saved and sent to the laboratory, where examination showed the constant presence of the Bence-Jones protein and no other. He grew steadily feebler, with increasing pain, referred to the ribs on the left side. Toward the end there was a development of nodes along the ribs over the precordium, with falling in of the sternum and great pain on breathing and coughing. There was enlargement of the lymphatic glands in the right groin, with great pain in the distribution of the anterior crural nerve. Glossitis was also noted.

No autopsy was permitted.

Case IV.—E. B., white, female, aged thirty-seven years. Admitted to the Johns Hopkins Hospital April 22, 1912. Died May 9, 1912.

Complaint: rheumatism.

Family History: Father supposed to have died of cancer. Previous History: unimportant.

Present Illness: Began six months before admission with onset of sudden pain in the right hip, which increased so that she was obliged to stop work two weeks later. Walked with great difficulty. After two months a similar trouble appeared in the left hip. Coincident with the joint trouble she noticed increasing nervousness, numbness of hands, and awkwardness. Appetite poor, occasional

vomiting unassociated with pain. Loss of 40 pounds in weight. Four weeks ago she noticed a painful lump in the right breast. Discovery of this lump was not elicited in taking the history, but during the physical examination.

Examination: Patient much emaciated. Slight general pigmentation, most marked in folds of the skin. Mild grade of ichthyosis simplex. Pupils react normally. Lungs clear. Heart normal. Hard, irregular mass in the right breast, with retraction of nipple and some puckering of the skin. Abdomen normal. Reflexes normal. No local or general glandular enlargement. Spine somewhat stiff. Some shortening of the right leg. Tender nodes on the sixth rib of the right side below the breast. Blood pressure, 140 mm. Hg.

Blood: Red blood cells, 4,000,000; leukocytes, 9200; hemoglobin, 74 per cent. Differential, normal. Wassermann, negative.

"*X*-ray examination shows carcinomatous metastases in head, ribs, both trochanters, both ilia, and right tibia. These metastases are slightly different from what one sees in simple ordinary metastases, in that the areas involved in the bones are sharply limited and do not seem to be invasive in character, as one ordinarily sees. The metastatic areas in the bone, at first glance, present the appearance more of a giant-cell sarcoma, as there is definite new-bone formation around the edge, showing an attempt had been made to limit the disease."

Urine: acid; clear; 1012 to 1018; no sugar; no casts; with heat and acetic acid there is a precipitation at 60° C., partial clearing on boiling, reprecipitation on cooling. Filtrate from this reaction gave no tests for protein. Total amounts of urine were studied for nine days, up to forty-eight hours before death. From the combined urines of this period the Bence-Jones protein was isolated by precipitation with two volumes of saturated ammonium sulphate and dialyzation until free from salt, the process being repeated three or four times until a clear, neutral, slightly amber colored fluid was obtained, which gave all the characteristic reactions for Bence-Jones protein in the pure state. This case will be reported in detail elsewhere.

The patient became rapidly weaker and semicomatose, with loss of control of sphincters, difficulty in swallowing, feeble, irregular heart, and death occured on May 9. No autopsy was secured, but a portion of the femur was removed for section.

"Section of bone and tumor showed epithelial cells of the glandular type in alveoli of different sizes and shapes, surrounded by a rather dense fibrous stroma. In this stroma there are two types of bone areas, old bone showing lacunar absorption by the cancer cells and typical islands of new-bone formation of the endosteal cell type. This was first described by von Recklinghausen as ostitis carcinomatosa."

III. General Consideration of the Urine. As has been so clearly demonstrated by Hopkins and Savory, the specificity of the reaction for Bence-Jones protein is dependent upon the relative stability of its compounds with neutral salts at the boiling temperature, and their instability at lower temperatures (45° C. to 60° C.). The saline concentration has a marked influence on the completeness of the reaction, following closely the laws defined by Hardy for globulins, but differing essentially in the temperature relation. Salts are similarly graded for Bence-Jones protein at 100° C. and for globulins at room temperature. It follows from the above consideration that in applying the heat and acid test to urine for the detection of protein it is important to heat slowly in order that the differences of temperature in the determination of precipitation may be apparent. Should coagulation begin well below the boiling point, more careful examination for the detection of unusual proteins (fibrinogen or Bence-Jones protein) are indicated. If this principle were impressed on students in their training, there is little doubt that many cases would be detected which are otherwise overlooked. In such instances of precipitation well below the boiling point, careful note should be made of any tendency toward clearing on boiling the specimen, and the test repeated with the aid of a water bath and a thermometer. Confirmatory tests are made by treating another specimen with a few drops of 25 per cent. nitric acid—when the initial turbidity in the cold is increased as we approach 60° C., and clears up more or less completely at 100° C., falling out again as the specimen cools. For further confirmation another specimen is treated with two volumes of saturated ammonium sulphate solution when a voluminous precipitation occurs, sometimes quite slowly. These tests are sufficient to establish the presence of Bence-Jones protein. Other tests for Bence-Jones body as it occurs in the urine and when isolated in the pure state may be found on reference to the table in Neuberg, *Der Harn*, 1911, i, 774. If serum albumin is also present it may be determined by first heating the acidified urine to 60° C. for one hour, cooling, filtering until perfectly clear, and boiling the filtrate.

At the outset of this investigation it was our intention to repeat the work of Magnus-Levy, Grutterink and de Graaf, and Abderhalden on the chemical constitution of the body isolated from our abundant material, but this field has been so satisfactorily covered by Hopkins and Savory as to render it unnecessary. A few notes may be made, however, on the relative advantages of the various methods of quantitative separation. For securing material without denaturing the protein, the salting with ammonium sulphate, dialyzing the precipitate, and repeating the process many times, probably yields the best result. This method has the objection that it is time-consuming, and does not free the protein from pigment.

It has been our experience that the urines containing this protein become dark on standing, even when preserved from putrefaction, and great difficulty was experienced in obtaining any precipitate which was not deeply pigmented. Various attempts were made to decolorize the urine before precipitating the protein by use of animal charcoal, Kieselguhr, or carbon black, but we could find no method which yielded a colorless filtrate which did not at the same time remove the greater part or all of the Bence-Jones body. Precipitates treated in thin dialyzing sacs of collodion with running water for weeks held tenaciously to the coloring matter. We also found, as has been noted by other observers, that the protein, when dried *in vacuo*, becomes dark, and these dried precipitates, in our experience, were never completely soluble in distilled water, which we consider an evidence of partial denaturization.

The alcohol precipitation would seem to be limited in its application to the treatment of small volumes, which may be rapidly handled, as the protein soon passes into an insoluble condition on prolonging its contact with the alcohol. Perhaps where facilities for refrigeration on a large scale are available the usefulness of this method may be extended.

For purposes of chemical analysis, where the denaturization, due to heating, is of no moment, we have devised a method which gives excellent results, especially in freeing the substance from pigment and leaving it as a fine dry powder.

The urine is filtered through paper, faintly acidulated with acetic acid, and placed in large bottles in the water-bath, which is kept at 60° C. over night. On removal from the bath, the greater part of the coagulum has settled to the bottom of the containers, which permits of decantation, or syphonage, of most of the supernatant urine. The precipitate is then repeatedly washed in the bottle by shaking with distilled water, and finally collected on a filter, and the washing continued until the filtrate is free from chlorine. The wet precipitate is then spread in Petri dishes in layers not more than 0.5 cm. thick, sealed, and placed in a freezing mixture of ice and ammonium chloride. The frozen material is rapidly transferred to a desiccator, packed in a freezing mixture. The desiccator is then quickly exhausted to a vacuum of 4 mm. or less, when the ice in the precipitate sublimes and is absorbed by the sulphuric acid, leaving the precipitate as a dry, crumbling mass, pale gray to white in color, which is easily pulverized. This material is insoluble in water, but readily dissolves in a dilute solution of sodium carbonate on heating, yielding a water-clear solution, from which the sodium carbonate can be easily removed by dialysis, leaving the protein in solution. Such a solution gives all the characteristic reactions for Bence-Jones protein in the pure state.

In Case I, the longest under observation, after the recognition of the proteinuria the amount excreted varied from 2 to 5 grams

per liter, with an output of 2 or 3 liters in twenty-four hours. In Case III the amount reached as high as 7 grams per liter, with an output of urine about the same as in Case I. The smallest excretion was in Case IV, in which the maximum was 1.5 grams per liter and the average 0.25 to 0.5 gram.

In one of our cases (Case I) we have observed spontaneous precipitation of the protein on standing for several months. These specimens of urine were found on bacteriological tests to be sterile, and the initial alkalinity considerably increased, though the urines were not ammoniacal. This phenomenon has been previously noted by Bradshaw[7] and Rosenbloom,[8] and will be reported fully elsewhere.

Polyuria was present at some time during the course of the malady in all of our cases except one (Case IV).

A striking feature to which attention has not heretofore been called is the great diminution in chloride excretion. The daily output in Case I was 2 or 3 grams; Case II, 5 grams; Case III, 1.5 to 4.5 grams, and in Case IV, 1.2 to 1.4 grams. In one case (Case IV) careful functional tests were made by Drs. Fitz and Rowntree. These showed a phenolsulphonephthalein excretion of 23 per cent. for two hours; lactose, 8 per cent.; iodide present after seventy-two hours; total chlorides, 0.15 to 0.18 per cent. of the amount ingested. In this case, also, serum albumin was at times present, but no casts were found. In the other cases the Bence-Jones body was the only protein present. In Case III casts were constantly present. None were found in Cases I and II.

IV. Biological Reactions. Although the chemical side of the Bence-Jones protein has been fairly completely covered in recent years, the biological investigations have been meager and somewhat conflicting. Borchard and Lippmann[9] have reported the detection of the body in the blood and serum of fasting dogs fed with the substance. In an alkaptonuric patient, Gross and Allard[10] noted a marked increase of homogentisic acid after feeding with this protein, in contrast to results obtained on feeding similar amounts of casein. After injection intravenously and subcutaneously, various authors have reported the presence of specific precipitins in the serum or blood. Rostoski found the reaction did not differentiate the Bence-Jones body from other proteins of human origin. Hopkins and Savory concluded that it is less powerful as a precipitinogen than blood proteins, but that its solutions react slightly with antihuman serum. Massini[11] reported complement fixation with highly potent sera, and was able to differentiate between the blood proteins and the Bence-

[7] Med. Chir. Soc., London, 1898, lxxxi, 259; British Med. Jour., 1898, i, 1136.
[8] Archives of Int. Med., 1912, ix, 255.
[9] Biochem. Zeit., 1910, xxv, 6.
[10] Zeit. f. klin. Med., 1907, xliv, 359.
[11] Deutsch. Archiv f. klin. Med., 1911, civ, 29.

Jones protein. Stokvis[12] noted the appearance of the protein in the urine of dogs after its injection intravenously or by the rectum. In our own experiments we have used the protein obtained by ammonium sulphate precipitation, and have been unable so far to secure a specifically active precipitin, finding only weak reactions of equal intensity for Bence-Jones and human blood serum, but are continuing the experiments with larger doses and with the substance in various states. In all our rabbits, injected intravenously for the production of precipitins, there was commonly anuria for twenty-four hours, followed, in some instances, by the excretion of the protein in the urine in the next forty-eight hours, while after the second injection none of the animals excreted the protein as such.

Intradermal skin tests for sensitization were made, with the same lot of material used for other biological tests, with negative results. The test was applied to a considerable number of individuals, normal persons, and others with various pathological conditions, 4 of whom had bone metastases from carcinoma and sarcoma, inclusive of Case IV. Instillation of the solution into the conjunctiva of Case I did not produce a reaction, nor was any obtained in a case of multiple sarcomatous metastases to the bones. Anaphylactic tests on guinea-pigs are in progress, and other biological investigations with this protein have been undertaken.

V. Summary. From the fact that the writers have observed 4 cases in fifteen months, it would seem that this type of proteinuria is probably more common than the literature would lead one to suppose.

Of these cases, 2 (Case I and Case III) were clinically multiple myeloma, and a third (Case II) was probably of the same type, although we have no objective proof. The remaining case (Case IV) was one of metastatic carcinoma from the breast, and is, we think, unique, as the case reported by Oerum[13] was associated with metastases from a gastric carcinoma. This case will be reported in detail elsewhere. It is especially interesting to note that the detection of the last three followed definitely the interest aroused among local physicians by the presence of the first case, which led them to test the urine of their patients more carefully. We should like to emphasize the fact that the recognition of the Bence-Jones body in the urine in each instance antedated any suspicion of the true nature of the malady, with the exception of Case IV, which was clearly associated with carcinomatous metastases. That this type of proteinuria may be present for some time before any clinical evidence of myelomatosis appears is shown by the first 3 cases noted.

[12] Nederl. Tidj. v. Geneesk, 1891, ii, 136; Maly's Jahr d. Thier. Chem., 1891, xxi, 412.
[13] Ugesk. f. Laeger., 1904, 5 s., xi, 559; Abst. Biochem. Zentrlbl., 1904-5, iii, 203.

In Cases I and III the palpable bone tumors developed only late in their course. In Case II death occurred from an intercurrent disease before the appearance of any symptoms suggesting bone involvement, and the skiagrams taken twenty days before death showed normal bone shadows. In Case I the *x*-ray pictures, as above noted, were imperfect, but showed a laminated rarefaction of the tibia. In Case III the radiologist made a diagnosis of an unfamiliar type of vacuolization in the bones prior to the appearance of any palpable bone tumors, while in Case IV an accurate diagnosis of metastatic carcinoma of the bones was made.

The blood picture in our cases showed nothing abnormal except a secondary anemia. All the patients were aged over fifty years, except the case of carcinomatosis (Case IV). In all there was evidence of great metabolic disturbance in the extreme emaciation. Spontaneous fracture of ribs occurred in 2 cases. The development of metastatic nodes in the soft tissues, as in Cases I and III, is unusual in myelomatosis. Both of these had also glossitis.

In connection with Case I, it is noteworthy that there was marked hypertrichosis, macroglossia, keratosis of the palms, and soles, and scleroderma. These point to some disturbance of the internal secretions which may have been coincidental. Fitz[14] has reported, however, Bence-Jones proteinuria in myxedema.

In regard to possible changes in the kidney, we can say nothing from the morphological standpoint, as we had no autopsies, but would merely call attention to the striking fact that the kidney was permeable for the Bence-Jones protein, but held back serum albumin (except just before death in Case IV), and in all cases there was a striking diminution in the chloride excretion. These would seem to indicate functional disturbance of the kidney rather than a true nephritis.

In closing we take opportunity to express our thanks to Drs. Wilson, Beck, Fitzhugh, and Futcher for access to their cases, and to Profs. Barker and Halsted for use of material in their services. Special thanks are due Dr. Baetjer for his interest in the radiographic studies, and to Drs. Fitz and Rowntree for the functional tests.

[14] Amer. Jour. Med. Sci., 1898, cxvi, 30.

FURTHER EXPERIENCES WITH THE COMPLEMENT FIXATION TEST IN THE DIAGNOSIS OF GONOCOCCUS INFECTIONS OF THE GENITO-URINARY TRACT IN THE MALE AND FEMALE.[1]

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In a previous paper[2] attention was drawn to the value of the serum diagnosis of gonococcus infections in general. We there showed that in chronic gonococcus infection, even though limited to the genito-urinary tract, an antibody specific for the gonococcus could readily be detected in the blood. Our experimental work showed that the secret of success lay in the use of a polyvalent antigen, on account of the fact that the different strains of the gonococcus seemed to differ considerably one from the other.

We then gave the results of the application of the test to a total of 324 human sera. These results showed that the complement fixation test (using a polyvalent antigen) for gonococcus antibodies should prove an addition to our methods of diagnosticating between the various chronic conditions arising from gonococcus infection and similar conditions due to other causes. In addition we pointed out that the complement fixation test might be a distinct aid in finally deciding as to whether a patient was cured of his or her gonococcus infection, inasmuch as the blood test was positive in a certain percentage of cases where other means of diagnosis failed.

Finally, we stated that, in our opinion, the facts at hand seemed to prove conclusively that a positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

Since then articles by Swinburne,[3] Keyes,[4] Schmidt,[5] and Gradwohl[6] have appeared corroborating our results in all essential particulars.

Technique. The antigen used at the present time is prepared as follows: The various strains of gonococci are grown on salt-free

[1] Read by invitation before the American Association of Genito-urinary Surgeons, Philadelphia, June 7 and 8, 1912.

[2] Amer. Jour. Med. Sci., May, 1911.

[3] Arch. of Diag., July, 1911.

[4] Amer. Jour. Med. Sci., Jan., 1912.

[5] Trans. Amer. Urol. Assoc., 1911.

[6] Amer. Jour. Derm. and Syph., Urinary Diseases, June, 1912.

veal agar, neutral in reaction to phenolphthalein; twenty-four-hour old cultures are washed off the agar slants with distilled water and the resulting suspension is heated for two hours in the water-bath at 56° C. It is then centrifugated and passed through a Berkefeld filter. No salt is added to this antigen until it is desired to use it, when it is made up to 0.9 per cent. strength by adding one part of 9 per cent. saline solution to nine parts of antigen.

The antigen is best preserved in small quantities in sealed tubes, heated to 56° C. for half an hour on three successive days, to insure sterility. If possible, the antigen is standardized with a known positive serum from a clinical case. If this is impossible, immune rabbit serum may be used, provided that the minimum amount of the serum which will completely fix complement is used. An antigen titrated with a highly immune rabbit serum may show perfect fixation in an amount that would fail to show any fixation with the average clinical case, on account of the lower antibody content of the latter. Antigens prepared as above will keep almost indefinitely if kept in sealed tubes free from contamination. We now use only the antisheep hemolytic system, but in other respects the technique is the same as described in our previous paper, except that we now use all the ingredients in one-tenth the quantity used in the original Wassermann technique for syphilis.

We may say that for the last few months we have used the gonococcus antigen prepared by Parke, Davis & Co., along with our own, and so far it has given satisfactory results.

Significance of a Positive and a Negative Reaction. As already stated, we found a positive reaction to be specific for the gonococcus with the sole exception of meningococcus infection.

Our positive results in meningococcus infection were obtained when using a highly immune anti-meningococcus serum prepared according to Flexner's method. We have since tested the serum of several patients suffering from cerebrospinal meningitis, with uniformly negative results. It would, therefore seem that, clinically, the complement fixation test for gonococcus infection is absolutely specific for the gonococcus. As is well known, the Wassermann reaction is not absolutely specific for syphilis. A positive reaction is obtained in various other diseases, notably leprosy, chronic malaria, frambesia, etc., probably due to the fact that the serum in these diseases contains abundant lipotropic substances. In the gonococcus complement fixation test we have a true antigen-antibody combination, inasmuch as the antigen is prepared from the specific infecting organism of the disease in question. In the Wassermann reaction we do not have this true antigen-antibody combination. The so-called antigens in the Wassermann reaction are present in the lipoidal substances of the tissues whether derived from luetic or non-luetic human subjects or animals. This probably accounts for the superior specificity of the gonococcus complement fixation test.

A negative reaction does not, of course, exclude the possibility of gonococcus infection being present, in the same way as a negative Wassermann reaction does not exclude the possibility of syphilitic infection. In this connection, however, there are two facts to be taken into consideration:

1. In the late lesions of syphilis, in common with the other infectious granulomas, there is a distinct tendency to the formation of a more or less well-marked connective-tissue capsule surrounding the lesion. As a result, there is arrested activity on the part of the spirochetæ, a less amount of toxin is elaborated, the connective-tissue capsule offers some resistance to the free absorption of toxins, and, as a result, there may be lessened antibody formation. This condition does not obtain in gonococcus infection, as the lesions here do not tend to become encapsulated.

2. The Wassermann reaction is definitely obscured by recent mercurial treatment. There is no treatment which thus obscures the complement fixation test for gonococcus infections. On account of these two facts we think that more importance may perhaps be attached to a negative reaction in testing for gonococcus infection than is to be attached to a negative Wassermann test for syphilis.

Time of Appearance of a Positive Reaction. A positive reaction is not to be expected earlier than about the fourth week of the disease, and then only in acute cases with some complication such as acute prostatitis, gonococcus arthritis, etc. For example, in one case of acute gonococcus arthritis coming on three or four days after the onset of the urethritis the blood was negative (though very slowly) on the twenty-first day, and strongly positive on the twenty-eighth day from the first appearance of the urethral discharge. In another similar case the blood was negative on the seventeenth day and strongly positive on the twenty-fifth day of the disease.

Time of Disappearance of a Positive Reaction after Cure. It is, of course, evident that the antibodies must persist in the blood for some time after the patient is actually cured. How long they persist is a difficult question to answer precisely. That they do not persist indefinitely we are quite certain. Torrey[7] has shown that the complement fixatives in the blood of a rabbit immunized to the gonococcus begin to be eliminated ten days after the date of the last inoculation and continue to be eliminated rapidly from the tenth to the fiftieth day, after which they are only found in small quantities.

Our own experiments with rabbits confirm these results. After the fiftieth day from the date of the last inoculation only a reaction can be obtained. This is a reaction to which we attach no importance.

[7] Jour. Med. Research, 1910, No. 1, p. 95.

Clinically, we have seen one case in which a two-plus reaction changed to a negative in five weeks after cure. The majority of cases, however, take somewhat longer. As a rule, we think a negative reaction should be obtained seven or eight weeks after cure. In other words, if a positive reaction is obtained seven or eight weeks after clinical cure we think that the patient should be looked upon as still harboring gonococci.

RELATIVE VALUE OF THE COMPLEMENT FIXATION AND BACTERIOLOGICAL METHODS OF DIAGNOSIS IN CHRONIC AND DOUBTFUL CASES, AND THE TECHNICAL DIFFICULTIES CONNECTED WITH THE TWO METHODS. As we have already stated, the complement fixation test is specific for the gonococcus. A positive reaction must therefore be looked upon as absolute proof of a focus of gonococcus infection somewhere in the body. What constitutes absolute proof of the gonococcus bacteriologically? Certainly not a smear stained with methylene blue. A Gram stain, properly made, can be accepted where the gonococci are abundant; but in chronic cases, with few organisms present, it cannot be accepted as absolute proof. Among the sources of error may be mentioned the Micrococcus catarrhalis; degeneration forms of Gram-positive cocci which not infrequently do not retain the Gram stain, and according to Adami[8] the Trichomonas vaginalis and some aberrant forms of the Bacillus coli. All authorities are agreed that in doubtful cases culture methods constitute the only absolute proof.

There is little doubt that the technique of isolating the gonococcus in culture is far more difficult than the technique of a complement fixation test. In the first place, the bacteriologist may err, as Dr. E. L. Keyes, Jr.,[9] well says, "through his own fault or through the fault of the clinician who submits the specimen to him, and the precision of his diagnosis depends upon a well-prepared specimen as much as upon his own skill." The prostate and vesicles must be thoroughly massaged and the specimen must be fresh, as it is probable that the gonococcus cannot be cultivated if allowed to stand in cool urine for half an hour. In addition, the gonococcus grows only on special media, and culture may fail on account of the presence of other rapidly growing organisms which either inhibit the growth of the gonococcus or render its isolation impossible. This is especially the case in women.

In connection with the complement fixation test, the only real difficulty lies in obtaining and carrying the various strains of the gonococcus necessary for the preparation of a good antigen. Apart from this, if the serologist carefully and frequently titrates the various reagents used in the test, a matter neither difficult nor time-consuming, the technique of the complement fixation test is comparatively simple.

All the above facts must be taken into consideration in judging

[8] Principles of Pathology, ii, 782. [9] Loc. cit.

as to the relative value of the bacteriological and complement fixation methods of diagnosis. In the presence of a positive complement fixation test and negative bacteriological findings, we think the fixation test should be accorded its full value. In the presence of a negative complement fixation test and positive bacteriological findings, we think the bacteriological findings should be accepted as correct only if the proof is absolute—namely, isolation of the gonococcus in culture.

In connection with the above statements the limitations of the complement fixation test, to be detailed later, are, of course, to be borne in mind. In all cases we think that in the interests of the patient both methods of diagnosis should be used.

I. GONORRHEAL URETHRITIS, GONOCOCCI PRESENT.

No. of cases.	Duration.	Reaction.
3	2 weeks	—
4	3 weeks, both urines cloudy	+
1	4 weeks, both urines cloudy	+
1	4 weeks, marked prostatic involvement	+++
2	4 weeks, gonococcus arthritis, 3 weeks	+++
1	5 weeks, both urines cloudy	+
2	6 weeks, both urines cloudy	+
1	7 weeks, prostatic abscess	++
2	8 weeks, both urines cloudy	++
1	8 weeks, prostatic involvement	++
1	8 weeks, second urine clean	—
1	10 weeks, second urine clean	—
4	12 weeks, prostatic involvement	+++

Remarks. The above illustrates the gradual development of a positive reaction.

In anterior urethritis, whether acute or chronic, a positive reaction is not obtained. Cases of urethritis remaining confined to the anterior urethra are, of course, rare. Most authorities agree that in the great majority of cases the posterior urethra is involved. One of Dr. Keyes' cases, however, had had urethritis for ten weeks. The first urine passed was slightly cloudy, the second urine, passed after the prostatic massage was quite clear and microscopic examination revealed no gonococci. There was a thin mucoid discharge at the meatus, in which gonococci were found, and they were also obtained in culture. Culture made from the urine passed after the prostatic massage was sterile. Here the infection was probably confined to a few glands in the fossa navicularis and there was not enough absorption of toxins to stimulate antibody formation. This case is cited here in order to bring out the point that probably a positive reaction is never found when the disease remains confined to the anterior urethra.

A weakly positive (one-plus) reaction first makes its appearance in the third week of the disease and only then when the posterior urethra is affected. In the ordinary case of acute antero-

posterior urethritis without complications running on to cure in six to eight weeks, the most that can be expected is a one-plus reaction. In the absence of complications a strong positive (two-plus) reaction does not make its appearance until the disease has lasted about eight weeks. A two-plus or three-plus reaction can be obtained as early as the fourth week, when there is some definite complication such as acute prostatitis, arthritis, etc. In fact, a three-plus reaction probably is not found when the disease is limited to the genito-urinary tract unless there is some definite implication of the deeper structure.

The fact that a positive reaction is not obtained in the early weeks of the infection, should prove an aid in differentiating between a fresh infection and the recurrence of an old, apparently cured, one. This also suggests possible medico-legal application of the test. Case XXI of Dr. Keyes'[10] series, illustrates this point. This was a married man who had infected his wife with gonorrhea some months previously. Both were treated and finally declared cured, and the blood test made some months later was negative in both. Two weeks later he returned, absolutely denying extra-marital exposure, but with a fresh gonorrhea two weeks old. Both he and his wife had the blood test made again, and both were negative. Four weeks later he was positive and she was negative, and she remained clinically cured. As Dr. Keyes says: "The development of a positive reaction in him showed the infection to be a fresh one due to extramarital exposure, in spite of his fervent denials." Dr. Keyes informs us that some six months later the husband finally confessed to the truth of the preceding statement.

Undoubtedly, however, the cases of greatest importance to the clinician, especially when the question of marriage arises, are those of chronic urethritis, prostatitis, and seminal vesiculitis following gonorrhea. Prostatitis is probably the most frequent and important complication. In many such cases we have obtained a positive complement fixation test when bacteriological methods have left us in doubt as to the presence or absence of the gonococcus. It is in such cases that we think the complement fixation test will prove an addition to bacteriological examination.

II. CHRONIC ANTEROPOSTERIOR URETHRITIS.

1. Gonococci present: In our experience in these cases a positive reaction is practically constantly found and we do not propose to enter into any detail here. We can only recall one case out of a great many examined in which the complement fixation test failed. This was a case of urethritis, followed in a few days by a multiple gonococcus arthritis. The blood was negative on the thirteenth, twenty-sixth, and thirty-sixth days of the disease,

[10] Loc. cit.

and positive on the sixty-first day. By that time, however, the patient had received eight injections of gonococcus vaccine which would have rendered the reaction positive in any case.

2. Gonococci doubtful: This group includes 5 cases in which both smear and cultural examinations were made, but in which the findings were inconclusive.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows fairly abundant sediment of pus. Smears show a few Gram-negative extracellular cocci. Plates show staphylococci and pseudo-diphtheria bacilli and a few Gram-negative cocci (gonococci?). Complement fixation test positive.

Case II. Gonorrhea fourteen months ago. Urine after prostatic massage shows scanty mucous sediment with a moderate number of pus cells. Smears show Gram-negative and Gram-positive bacilli, Gram-positive cocci and very few Gram-negative cocci. Plates show Gram-negative bacilli, staphylococci, and streptococci. Complement fixation test positive.

Case III. Gonorrhea five years ago. Urine after prostatic massage shows moderate number of pus cells and a few Gram-negative extracellular cocci. Plates contaminated. Complement fixation test positive.

Case IV. Gonorrhea three years ago. Urine after prostatic massage, shows slight mucous sediment, few pus cells, and a few atypical extra-cellular Gram-negative cocci. Plates sterile. Complement fixation test negative.

Case V. Gonorrhea three years ago. Urine after prostatic massage shows moderate number of pus cells. Smears show many Gram-positive cocci and a few Gram-negative extra- and intra-cellular diplococci. No Gram-negative cocci. Complement fixation test positive.

3. Gonococci negative, both in smear and culture. Nine cases giving a history of gonococcus infection from nine months to fifteen years previously were negative by the complement fixation test thus agreeing with the bacteriological examination. Two cases gave a positive complement fixation test.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows a moderate number of pus cells. Smear shows Gram-positive cocci. No Gram-negative cocci. Plates show staphylococci and streptococci. No Gram-negative cocci.

Case II. Gonorrhea three months ago. Urine after prostatic massage shows few pus cells. Smears show Gram-positive cocci and Gram-negative bacilli. Plates show streptococci and Gram-negative bacilli. In this case the positive complement fixation test was very possibly a fading reaction.

4. Gonococci negative in smear only, cultural examination not made. Six cases, giving a history of gonococcus infection from seven months to five years previously were also negative by the complement fixation test. One case, giving a history of gonococcus

infection two years previously, was positive by the complement fixation test.

5. Cases in which gonococci were not searched for. These cases all had symptoms of chronic urethritis believed to be postgonorrheal. The duration of the urethritis varied from two to fifteen years. Thirty-one cases were examined, of which 10 or 32.2 per cent. gave a positive reaction.

The cases included in groups 2, 3, 4, and 5, were all regarded clinically as postgonorrheal. If now we group all these cases together, we find that out of 54 cases examined a positive result was obtained in 17 or 31.4 per cent. These figures closely correspond with those reported by Keyes[11] in postgonorrheal urethritis, in 26 cases carefully examined by smear and culture gonococci were found in 8 or 30.7 per cent. In a number of our cases, however, the result of smear and cultural examinations was suspicious, but inconclusive, as cited in group 2, whereas the complement fixation test was definitely positive or negative. Herein, in our opinion, lies one great advantage of the complement fixation test.

III. VERUMONTANUM DISEASE. GONOCOCCI NOT FOUND.

Twenty-two cases of disease of the verumontanum have been examined. Of these, 21 admitted gonorrhea from one to ten years previously. Four of the 21 gave a positive reaction and 17 a negative reaction. One case, cited in our previous paper, absolutely denied gonorrhea, but had given a positive result on two separate occasions. After six months' treatment he was found to be negative.

IV. CHRONIC PROSTATITIS

1. Gonococci present: Three cases were examined, all of which gave a positive complement fixation test.

2. Cases giving a definite history of gonorrhea—gonococci not searched for.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
5 weeks to 1 year ago	31	20	11
2 years ago	19	9	10
3 years ago	12	5	7
4 years ago	5	2	3
5 years ago	7	0	7
6 years ago	3	2	1
7 years ago	5	2	3
8 years ago	2	1	1
10 years ago	3	1	2
12 years ago	6	3	3
14 years ago	1	0	1
20 years ago	3	1	2
30 years ago	1	0	1
3. Gonorrheal history doubtful	9	2	7
4. Gonorrhea denied	2	0	2

[11] Loc. cit.

In group 2 we have a total of 98 cases of chronic prostatitis in which a definite gonorrheal history was obtained. Of these, 46, or 46.9 per cent., gave a positive reaction.

It will be noted that we have obtained positive results in cases where the last gonorrheal infection was stated to be anywhere from six to twenty years ago. We, of course, do not vouch for the accuracy of the patients' statements in that regard. Opinions vary greatly as to the length of time the gonococcus may persist in the genito-urinary organs of the male and female. We feel that a patient giving a positive complement fixation test should be looked upon as still harboring gonococci irrespective of the date of the last gonorrheal infection.

V. SEMINAL VESICULITIS.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
6 months ago	1	0	1
2 years ago	3	1	2

VI. CLINICALLY CURED CASES.

In this group we have included only such cases as have been looked upon as clinically cured for at least three months. This was done so as to avoid the possibility of including cases which actually were cured but might still present a fading reaction.

We have examined in all 165 cases, of which 22, or 13.2 per cent., gave a positive reaction. These figures correspond closely with those reported by Schmidt[12] at a recent meeting of the American Urological Society. Out of 42 cases examined he obtained a positive result in 5, or 11.9 per cent. Keyes[13] estimates about 4 per cent. of clinical error in cases apparently cured, basing this statement on the results of laboratory investigation of 86 patients clinically cured of urethral gonorrhea. Thirty-six of his cases were examined by the complement fixation test, and 77 by smear and culture.

In our previous paper we reported 43 per cent. of positive results in cases of this group. Our first series contained all cases examined from the very beginning of the investigation, before we had any definite idea of the possibilities of the test and cases were classed as clinically cured which more rigid examination would probably have excluded from that group. The cases here reported have all been very thoroughly examined before being classed as clinically cured and we think that 13.2 per cent. represents fairly accurately the clinical error in such cases. The importance of these results when the question of marriage arises needs no emphasis here.

[12] Jour. Amer. Med. Assoc., April 27, 1912, p. 1307.

[13] Loc. cit.

VII. WOMEN.

The diagnosis of gonococcus infection in women is well known to be very difficult and uncertain, and bacteriological methods of diagnosis are not of any great assistance, except in the acute forms which are relatively rare. In subacute and chronic forms, gonococci are generally very scanty. They are to be found more particularly in the discharge from the urethra and cervix. However, the great number and variety of other organisms present in such discharges renders the absolute demonstration of the gonococcus exceedingly difficult both in smear and culture. Very often both clinical and bacteriological examinations leave one in doubt and the diagnosis of chronic gonococcus infection must be only a probable one. Hence, we feel that in women the complement fixation test should prove a distinct addition to our means of diagnosticating chronic gonococcus infection.

Extent of Involvement Necessary to Obtain a Positive Reaction. It will be remembered that in discussing the question of gonococcus infection in the male, it was stated that a positive reaction was not to be obtained if the disease remained confined to the anterior urethra. There had to be at least some involvement of the posterior urethra in order to obtain a positive reaction. In gonococcus infection in the female, the organs chiefly involved are the urethra and Skene's glands, Bartholin's glands, the cervix, the uterine tubes, ovaries, and peritoneum. The vagina very commonly escapes, especially in the adult. In children the vaginal mucosa is much more likely to be infected, as in the young, the pavement epithelium is softer and more like columnar epithelium. Hence, the frequency of gonococcus vulvovaginitis in children.

We have obtained positive reactions in cases of peritonitis, in tuboövarian disease, and in disease of the cervix.

We have also obtained a positive reaction in 2 cases of vulvovaginal abscess, but in the absence of abscess formation, we doubt if a positive reaction will be obtained unless there is some infection of the cervix. In other words, we think a negative reaction will probably be obtained if the disease is limited to the urethra, Skene's glands, and Bartholin's glands. Such cases are doubtless rare, as in the great majority of cases of chronic gonorrhea in the female the cervix is involved. Still we feel that the possibility deserves mention here. In gonococcus infection in young children, the vulva, urethra, and vagina are chiefly affected; only rarely are the cervix, corpus uteri, and tubes involved. We have examined 10 cases of vulvovaginitis in children aged under five years. In all the gonococcus was demonstrated in smear and culture. In all the complement fixation test was negative. This tends to support our opinion that a positive complement fixation will not be obtained unless there is involvement of the cervix.

The important role which the gonococcus plays in the production of pelvic disease in women, scarcely needs mention. Destructive inflammation of the tubes and ovaries, with peritonitis, is common, as is also gonococcus infection of the bladder with secondary ascending infection of the ureters and kidneys.

Finally, on every general maternity service cases of gonorrheal ophthalmia occur from time to time. Statistics show that even with the use of silver nitrate in the eyes, this disease occurs as often as once in every 200 cases. Apart from the possible serious effects upon the eyes of the child itself, there is always great danger of the infection spreading to other infants and nurses. Therefore, on account of the unreliability of the smear and cultural methods of diagnosis of subacute and chronic gonococcus infections in women, we think that the complement fixation test should find a distinct place in gynecological conditions, and that on general maternity services it will be of use in the prevention of gonorrheal ophthalmia.

We have not applied the test as extensively in diseases of the genito-urinary tract in the female as we have in the male. This was principally on account of the fact that our chief object was to study the possibilities and limitations of the test. This could be done much more satisfactorily in the male because the course and development of gonococcus infection is much more readily studied in the male. Furthermore, the complement fixation test could be more thoroughly controlled by bacteriological examination in the male than in the female.

The statistics which follow give, however, a fair idea of the field of usefulness of the complement fixation test in gynecological conditions.

Clinical diagnosis.	Positive.	Negative.
Urethritis and endocervicitis;		
(*a*) Gonococci present	9	0
(*b*) Gonococci not found	8	3
Gonorrhea clinically cured	1	4
Chronic gonorrhea, gonococci not found	2	0
Gonorrheal vulvovaginitis; girls under five years, gonococci present	0	10
Salpingo-oöphoritis	9	3
Pyelitis clinically considered gonorrheal	2	6
Vulvovaginal abscess; gonorrheal	2	0
Pelvic peritonitis	3	1
Pregnancy; gonococci present	1	0
Pregnancy; gonococci not found	14	40
Miscellaneous cases from the clinic; lacerations, displacements, etc.	13	50
Pyosalpinx	3	4
Pelvic abscess	0	2

One case clinically diagnosticated as pyosalpinx, and giving a negative complement fixation test, was found at operation to be a case of cystic ovary with normal tubes.

One case diagnosticated as pelvic abscess, and giving a negative

complement fixation test, was found at operation to be a tubo-ovarian abscess from which the colon bacillus was obtained in pure culture.

1. CONCLUSIONS. A positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

2. A negative reaction does not exclude gonococcus infection but, for the reasons stated, should be accorded considerable importance.

3. A strong positive reaction is not to be expected earlier than about the fourth week, and then only in very acute cases with some complication.

4. A positive reaction is not obtained if the disease is limited to the anterior urethra.

5. A positive reaction does not entirely disappear until seven or eight weeks after cure.

6. In other words, if a strong positive reaction is obtained seven or eight weeks after apparent clinical cure, the patient should be looked upon as still harboring gonococci.

7. In chronic cases, isolation of the gonococcus in culture is the only absolute, bacteriological proof of gonococcus infection.

8. The technique of a complement fixation test is simpler than that of isolation of the gonococcus in culture and the possibilities of error are less.

9. In cases regarded clinically as postgonorrheal, a positive reaction is obtained in 31.4 per cent.

10. In 62 cases of chronic prostatitis giving a history of gonococcus infection within three years, a positive reaction was obtained in 54.8 per cent.

11. In 165 cases looked upon as clinically cured for at least three months, a positive reaction was obtained in 13.2 per cent.

12. In women, a positive reaction is probably not obtained unless there is at least some involvement of the cervix.

13. On account of the unreliability of the bacteriological diagnosis of gonococcus infection in women, the complement fixation test should prove of special usefulness in gynecological conditions.

NOTE.—Since this paper was written, other articles on the subject have appeared, as follows: Smith, Lancet-Clinic, Aug. 3, 1912; O'Neil, Boston Med. and Surg. Jour., Oct. 3, 1912; Gardner and Clowes, New York Med. Jour., Oct. 12, 1912. These articles also corroborate the results of previous workers.

INDICANURIA.

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The presence of excessive amounts of indican in the urine is so frequent that we have all seen hundreds of such cases. I have taken occasion to go over my records of all patients seen in 1911 whose urine showed an excess of indican, and will present the observations which I have made from the study.

Indican, or the indoxyl sulphate of potassium, as is well known, is non-toxic. The indol from which it is formed is but slightly toxic, Herter claiming that small doses may produce in man frontal headache, mental irritability, insomnia, etc. Wooley and Newburg, in a preliminary report of their experiments on the result of the injection of animals with indol, found that examination of the adrenals showed the medulla hyperplastic and apparently hypertrophic, and that the evidences of chromaffin activity increased in proportion to the number of injections. They also found slight interstitial changes in the kidneys.

It may be, therefore, that, *per se*, excessive indol absorption from the intestine over a considerable length of time may, by stimulating the adrenals to increased secretion, be instrumental in producing arteriosclerosis and chronic nephritis. Be that as it may, we make use of the indican test because we believe that in most cases the various products of bacterial decomposition, or bacterial digestion as expressed by Combe, of proteids in the intestines, that is, the aromatic bodies (including indol, skatol, phenol, and the cresols), and toxalbumins develop and are absorbed with a certain relationship. Since we have no means at present of determining the quantity of the more definitely poisonous toxalbumins, we are forced to estimate their amount by the degree of putrefaction, as evidenced by the amount of indican excreted in the urine.

In my laboratory the ordinary test for indican employed is: 10 c.c. HCl, 10 c.c. of 1 per cent. solution of potassium chlorate, 3 drops of which is added to the urine and shaken up with 5 c.c. of chloroform. The blue color in the chloroform indicating an excess of indican is arbitrarily graded as to intensity from plus one or sky blue to plus six, the highest grade which we encounter, a very black blue.

Indol results from bacterial digestion or putrefaction of proteids, the bacteria taking up the work of splitting the proteid molecule where the enzymes have left off. It is fairly certain that the lower ileum is the chief laboratory for the formation of this end-product, and that the principal absorptive seat is the colon. Considerable

putrefaction can undoubtedly occur without the occurrence of indicanuria, due probably to non-absorption from the colonic mucous membrane or to some protective mechanism in various organs of the body, as the liver. On the other hand, loss of continuity of the surface of the colon may result in considerable quantities of indican being present in the urine where the degree of putrefaction could hardly be considered enough to account for it. While not all cases of intestinal putrefaction result in indicanuria the writer believes that excessive indican in the urine always indicates abnormal functioning, and that the cause should, if possible, be found and eliminated.

During the year 1911, 148 patients showed indican transitory or more persistently. The cases were about equally divided between the sexes, 73 occurring in females and 75 in males. Usually the indican was incidentally present during treatment for other gastro-intestinal conditions. In some it was accidental or transitory, in some recurrent, in others more or less constant, a definite part of the clinical picture, but still associated with other pathological processes, and in several it was present without evident cause. The latter are the cases of true indicanuria, idiopathic or perhaps to be classed as pure intestinal auto-intoxication. I agree with Baar, who considers these cases of true intestinal auto-intoxication as rare. He specifies that examination of the whole body, the stomach contents, the feces, and blood must yield no abnormal findings.

Of the new patients consulting me in 1911, 89 showed indican in the urine on the regular routine examination at the time of consultation. Of this number 24 showed plus 1, 30 plus 2, 22 plus 3, 9 plus 4, 3 plus 5, 1 plus 6.

In a former paper the writer stated that indicanuria is several times more prevalent in Washington from January 1 to July 1 than during the remaining months of the year, the explanation for which will be mentioned later. Of the 148 cases, 92 occurred in the first six months of the year. A consideration of the distribution of the 89 new patients does not indicate this state of affairs so plainly. They consulted me as follows: In January, 10; February, 10; March, 6; April, 10; May, 7; June, 6; July, 7; August, 11; September, 5; October, 10; November, 3; December, 4. Of 59 who developed it during the period of observation, 48 occurred between January 1 and July 1.

One thing seems certain with reference to the season and that is that excessively hot weather does not seem to play a noticeable part in causing or increasing the production of indican. June and July of last year were very hot months, and yet only 6 or 7 of these patients applied for treatment during these months.

Analyses of the cases show no particular etiological factor common to all or even a considerable number of the patients. Nearly all

of the more common forms of gastro-intestinal diseases were represented. Of the 113 patients in whom gastric analyses were made 46 showed hyperacidity, 25 subacidity or anacidity, and 42 normal figures. Whether the considerable number showing increased figures for acidity has any significance or not has not been determined. Nor do we know in how much the hyperchlorhydria is one of the causative factors and how much a result of the toxic condition. Baar found ulcer with hyperacidity to be always accompanied by excessive indican and attaches such importance to the combination of hyperacidity and indicanuria as to use it as a diagnostic sign. He says that provided ulcer of the stomach and duodenum can be excluded, hyperacidity with indicanuria indicates an extragastric lesion as appendicitis or cholecystitis. My own observations are not in accord with this view. Not more than one-third of my ulcer cases treated during the last year showed excess of indican. On the other hand, my records show a number of instances in which indican and hyperacidity were present, probably from the same cause, loss of nerve tone, and in which there has never been any suspicion of extragastric inflammatory trouble.

Uncomplicated constipation does not seem to be instrumental in causing indicanuria, although a few observers have noted a considerable excess of indican in a majority of their patients with chronic constipation. Only a small number of my patients seeking relief for chronic constipation showed indican in excess. The condition of the bowels in my series was as follows: Constipation, 60; looseness, 15; constipation alternating with diarrhea, 13; and the balance normal. Many are classed with those having constipation who are merely of the constipated tendency, some of them having daily bowel movements unaided most of the time, others having daily movements, with the aid of medicine, while some were obstinately constipated. Several of the patients with the most persistent and marked indicanuria came in the class of those having normal daily bowel movements. At all events, it is a question whether the condition of the bowels should be discussed under etiology or symptomatology, as it is more than likely that a considerable part of the constipation or diarrhea may be the result of the intoxication and not one of its causes.

Obstipation resulting from obstruction of the transverse colon or above it can result in profound indicanuria, but this diminishes as the obstruction is lower down and affections of the lower part of the gut are only exceptionally complicated by indicanuria.

Although not represented in my series, it is well known that indican is greatly increased in peritonitis, typhoid, and cholera. Also occasionally responsible are ozena, caries, and other pus collections. Baar has found that after all operations in which the intestinal wall was cut or the organs roughly handled indican was present in the urine for a week.

Although some observers have claimed that affections of the liver are frequently productive of indicanuria, the writer is still of the opinion previously expressed, that the indicanuria is a complication and not a direct result unless in case of extreme hepatic insufficiency.

Probably the most frequent cause of the putrefaction resulting in indicanuria, according to the writer's opinion, is a combination of improper diet—most often excessive quantity—and a run-down condition with loss of nerve tone. As has been mentioned, this fact has been demonstrated by the greater number of cases encountered in Washington during the period of the year furthest from the vacation or at the end of the busy season.

Is there a symptom-complex which will enable us to say that the patient is suffering from an intoxication manifested by indicanuria? There are some who do present typical and complete clinical pictures, but the majority in my series had but a few of the symptoms. These, while not always characteristic, were usually indicative of an intoxication by a poison having especial predilection for the nervous system. Close analysis was made of the response to the question, "What symptoms trouble you most?" and then to specific questions concerning headache, dizziness, etc.

The typical symptom-complex consists of vertigo of varying degree, dull headache, languor, drowsiness, depression, lack of ambition, inability to concentrate the mind, insomnia, or sleep that is not restful, easy fatigue, irritability, gas in the bowels, muscle pain and cramps in the legs, cold hands and feet, and fetid breath. In many there was a partial loss of coördination. None of these symptoms were constant, but nearly all the cases exhibit some of them. However, a few cases had no symptoms at all. Mr. E. F., whose case will be mentioned below as illustrating another point, had indicanuria of the greatest degree almost constantly for twelve years, and yet most of the time felt in perfect health.

The one symptom which in the largest number of patients was complained of with the greatest degree of regularity was gas formation in the bowel, indicating the underlying putrefaction. Ninety-six patients were troubled with this symptom.

Early fatigue was mentioned among the most troublesome symptoms by 32. This state of tiring easily was met with in nearly all of the patients, but the routine of questions asked in my office does not include this question specifically. These 32 volunteered the information without questioning. Allied symptoms of constant languor and depression usually accompanied the fatigue, but 17 patients complained of these symptoms without noting the fact that they tired easily.

The patients were questioned specifically concerning headache and dizziness. Sixty had headache in some degree or form. Occa-

sionally the pain would be neuralgic in character, but more often a dull frontal ache. In some it occurred comparatively rarely, while in others it appeared almost daily. Frequently the pain was found to be worse in the morning.

Fifty-five patients of the series were troubled with dizziness. This also varied in character and time of appearance. In some it manifested itself merely by a transitory light-headedness. In others there would be sharp attacks while in some the vertigo would be almost constant, and so severe as to cause staggering.

The severity of the headache and dizziness as well as of the other symptoms does not seem to bear a direct relationship to the degree of indican excreted, but perhaps rather is dependent upon the tolerance of the patient for the poisons.

Insomnia was noted not infrequently. Again, often though the patient could go to sleep without any difficulty, it would not be restful or refreshing, and there would be a feeling of exhaustion in the morning.

One of the evidences of intoxication which, although it occurs comparatively rarely, seems to be quite characteristic, is pain in the legs and perhaps other muscles. There is no soreness to the touch, as a rule, but a decided pain varying from a cramp-like condition of the muscles of the calf to a steady rheumatic ache.

Other nervous symptoms noted in my series are loss of memory, uncertain feeling in the head, rush of blood to the head, inability to think while at work, lack of will power, phobias of various sorts, hazy spells during which things seem far off and veiled, feeling of panic, loss of consciousness for short period, palpitation of the heart, faintness, cold hands and feet, numbness in hands, loss of taste and smell, black specks before the eyes, free perspiration, and irregular muscle twitching in different parts of the body, occurring especially during sleep.

From the foregoing it may be seen that the toxins affect the nervous system in a variety of ways. None of the symptoms are entirely characteristic, but a combination of some of them is very suggestive, and we should be able to make a tentative diagnosis before examination of the urine. Often we are misled both ways. It not infrequently happens that in a patient with decidedly suggestive symptoms repeated examination of the urine fails to reveal excess of indican, and, on the other hand, quite marked amounts of indican are many times present without any symptoms to indicate such a state.

Examination of the patients in my series revealed, in addition to the many conditions present from accompanying disorders, some which are more or less frequently met with as a result of the intoxication itself. The skin was often found pale and dry, and various skin eruptions were not uncommon. Nearly all of the series had an anemia more or less marked, the average being about 72 per cent. hemoglobin.

Bram has recently claimed that indicanuria and albuminuria are not commonly found at the same time, and that the presence of one in considerable amount would indicate the other to be absent or in small quantities. He makes these deductions from 500 examinations at the Medico-Chirurgical and Jewish Hospitals of Philadelphia. One hundred and eighty-seven of the specimens of urine showed albumin but no indican; 210 showed indican but no albumin; 4 had albumin with a questionable trace of indican; and 2 had indican with a questionable trace of albumin.

On the other hand, Daremberg found that 95 per cent. of his patients with indicanuria had also an albuminuria. In my series it was exceedingly common to find albumin, usually in faint traces and hyaline casts indicative of a chronic interstitial change, and, indeed, it would be surprising if some change were not induced in the kidney by long-continued excretion of poisons.

One patient who had large amounts of both indican and albumin continuously presented such an interesting condition that his history will be given with some detail:

Mr. E. A. F. consulted the writer January 31, 1911. He was a newspaper man, aged thirty-one years, with a history of having had marked albuminuria and indicanuria for thirteen or fourteen years continuously. Frequent examination by competent observers indicated that the two conditions varied with each other. Most of the time he had no symptoms, even when indican and albumin were both present in large amounts, but for the previous six months he had had gas in the stomach and bowels off and on accompanied by intestinal distress and attacks of headache. His bowel actions were fairly regular, but with a tendency to looseness. He always felt worse just before the bowels moved. He also complained of indefinite pains in the calves of the legs after walking. He had no dizziness, and was always able to carry on hard work.

On examination his physical condition was apparently excellent, being negative except for a slight aortic systolic heart murmur. His blood pressure at the time of the first examination was 162 mm. Examination of the stomach contents showed increased figures, free HCl, 76; total acidity, 90. His hemoglobin, 78 per cent. The urine on first examination showed specific gravity, 1020; albumin, 6.5 per cent.; indican, plus 2; numerous hyaline and finely granular casts. His weight was 174 pounds. Throughout February daily examination of the urine was made, the indican varying from plus 1 to plus 6 and the albumin keeping pace with the indican. During the last half of the month the patient began to respond to the treatment, and the indican for a period of several weeks was either normal or but slightly increased, while the albumin sank to 1 per cent.

March 3. After harder work his indican again abruptly rose to plus 4, persisting at that figure for nearly a week, when it was

again controlled and gradually sank to normal again, then increasing correspondingly.

March 23. The effects of nerve strain in handling Congressional reports for his paper again became manifest, and the indican did not again become normal for three months, when he took his vacation. Congress remained in session unusually long during the spring of 1911, and his work was so arduous as to offset any advantages secured by the constant treatment. All symptoms had ceased after the first two weeks of treatment by hygienic measures, diet, and irrigations, and there was no return of them until the indican again increased.

During the three months of constant and severe indicanuria various methods were tried in addition to the irrigations, all without influencing the amount of indican in the slightest, although each change would give the patient a feeling of well-being. Cultures were made of the stools and an intensely acid colon bacillus was found to make up about 98 per cent. of the bacterial content of the bowel. Vaccines were administered several times. Rapid variations in the diet were made, with the object of changing the bacterial flora of the intestines. Hot baths were tried. Bile salts were administered. Finally thyroid extract was tentatively tried a few days before he went on his vacation, and apparently diminished the amount of indican considerably. While on his vacation of several months he took on his own initiative the thyroid almost constantly. On his return to the city in the fall he had lost weight, going from 174 to 144½ pounds as a result of the thyroid, but he felt fairly well. He still had some increase in indican excretion, about one-half of the amount he had before going away.

The cure for indicanuria must come through measures preventing the formation of toxins and the elimination of those already formed. In the treatment it is necessary first to eliminate if possible the primary cause of the excessive putrefaction and to prescribe treatment for any disorder of the gastro-intestinal canal whether causative or associated with the production of indican. Further consideration will not be paid to this, as it includes the treatment of nearly all of the gastro-intestinal disorders. In a not inconsiderable number of the cases the excessive production of indican ceased without direct measures being instituted for its treatment when the mental strain was removed; other cases have taxed our ability to the utmost before they have responded to treatment.

Measures directed toward the putrefaction and indicanuria itself consist of general hygienic directions, diet, exercise, irrigation, and occasional medication. Purgatives not only do not cause a diminution of the indican, but may even be followed by increased excretion. Irrigations are nearly always found necessary when direct treatment for the indicanuria is needed. Different solutions have been used to meet varying conditions in my series. Salt

solution, soda, argyrol, and ichthyol have all given admirable results. Ichthyol solutions often seem effective when others have failed.

In arranging the diet we have greatly reduced the proteid food, thereby removing much of the material available for the putrefaction. Frequent changes in diet have been tried, with the idea of producing unfavorable conditions for the growth of the putrefactive bacteria. Although buttermilk has been given to many, the writer's experience with it, and the artificial preparations of the lactic acid bacilli has not been such as to cause any reliance to be placed in these preparations *per se*.

No one point has been found to be of more importance in those many cases where overwork is a factor than a restoration of nerve tone, as by a vacation spent under ideal conditions in the mountains. Some of my patients have indicanuria which recurs with some degree of regularity in the spring, disappearing after a thorough bodily and mental rest.

In the majority of my cases cure of the condition has been comparatively easy, but in the occasional true auto-intoxication the progress has been slow and at times discouraging. Although not invariable, it has been our experience that the longer the duration of the indicanuria the greater the length of time it persists under treatment.

ADENOCARCINOMA OF THE THYROID, WITH METASTASIS TO THE CERVICAL GLANDS AND PITUITARY: A CONTRIBUTION TO THE PATHOLOGY OF ABNORMAL FAT FORMATION.

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The underlying pathology of excessive and aberrant fat formation has in recent years been the subject of much investigation. Following the publication, in 1888, of the original article by Dercum on "Adiposis Dolorosa," many cases were placed on record as belonging to this syndrome which in the light of the newer researches into the pathology of fat formation have been segregated into other groups. The general tendency has been to divide the various pathological forms of fat formation into groups according to the clinical picture. The following clinical forms have been described: (1) Dercum's syndrome—adiposis dolorosa, (2) adiposis tuberosa

simplex (Anders), (3) symmetrical adenolipomatosis (Launois and Bensaude), (4) adipositas cerebralis (Froelich), (5) adipositas pinealis (Marburg), (6) nodular circumscribed symmetrical multiple lipomatosis, (7) adiposis secondary to true or neuropathic edema.

Cases of adiposis dolorosa are often met with and constitute a fairly definite clinical picture. Painful indurated areas in the fat tissue associated with asthenia, mental symptoms, and psychic manifestations, constitute the four cardinal symptoms. Anders separated from this group a series of cases showing indurated tumor-like masses in the fat tissue without pain or tenderness, and without asthenia or psychic manifestations.

Launois and Bensaude under the title of l'adéno-lipomatose symétrique à prédominance cervicale reported a series of cases of symmetrical fat deposits about the neck and shoulders that deserved special clinical consideration. Many similar cases had already been reported in the literature, beginning with that of Brody in 1846. Madelung, who wrote the first systematic treatise on the subject, considered the condition as a special clinical variety of lipomatosis. Launois and Bensaude, after digesting the literature, came to the conclusion that symmetrical adenolipomatosis, adenolymphocele, segmentary edema of Debove, neuropathic pseudoelephantiasis of Mathieu, and supraclavicular pseudolipoma were not necessarily identical, but belonged, nevertheless, to the same morbid group. The adenolipomatosis cases of Launois and Bensaude were characterized by symmetrically placed diffused fat masses localized to the region of the neck, the axilla, and the trunk, and associated with asthenia, mental irritability, apathy and hypochondria, enlargement of the spleen, acceleration of the pulse, and decrease of small mononuclear cells. These fat masses even when of great size may be associated with general emaciation. Microscopic examinations of incised portions have shown the presence of large and sclerosed lymphatic glands in the fatty tissue. An increase and diminution in the size of the fat during its development has led Launois and Bensaude to consider the disease to have its origin in the lymphatic system.

In the only autopsy on record, Dieulafoy showed no lesion in the nervous system, but found cirrhosis of the liver and spleen and pancreas, tuberculosis of the peritoneum, adenomatous hypertrophy of the thyroid, with an enlarged and congested pituitary body. The fat masses showed no evidence of lymphatic tissue, and the nodules noted were evidently due to an invasion of connective tissue. Lyon includes an autopsy, reported by one of the authors of this paper with Dercum, as belonging to this group. This will be considered later.

Adiposis cerebralis. This condition described by Froelich has a very close analogy to adiposis dolorosa. In its simplest form it consists of an excessive general adiposis developing during the

course of a brain tumor, which in most cases has been found at autopsy to involve the pituitary body, but which in one case was found to involve the pineal gland (Marburg). A close association has been found in this group of cases with defective development of the genital organs. E. von Eiselberg has reported marked improvement and apparent cure after the removal of the pituitary body in 2 cases.

Nodular circumscribed symmetrical lipomatosis. Multiple isolated lipomatous tumors have occurred symmetrically placed in different portions of the body. On account of the symmetrical arrangement and on account of the association of the tumors, with tabes, general paralysis, sciatica, etc., it has been assumed that the nervous system and more particularly the trophic centres in the spinal cord were the cause of the affection. There is, however, practically no evidence to support such a theory. As many as 2000 of these lipomatoma have occurred in the same individual (Launois and Bensaude).

Adiposis secondary to true or neuropathic edema is a gradual transition and transformation of tissues which are the seat of chronic edema to at first pseudolipomatous, and later, true lipomatous tissue. Two groups may be identified: (1) Neuropathic edemas which most often give rise to the pseudolipomatous state, and according to Strübing, are closely related if not identical with the edematous swelling of adiposis dolorosa. (2) True edemas sometimes noted on the paralyzed side of hemiplegics with failing cardiac or renal function. If the patient lives sufficiently long they may become transformed into pseudolipomatous tissue, which does not pit on pressure and which has all the characteristics of subcutaneous adipose tissue.

From a clinical standpoint the above groups stand out fairly clear and distinct. It would not be a difficult matter to form new subgroups. When, however, we consider the underlying pathological factors we find for the most part somewhat similar organic changes in practically all of the above groups. In adiposis dolorosa the first group to be studied postmortem, our attention was directed to the region of the ductless glands and the generative system. In both cases upon which one of us performed the autopsy, lesions of the pituitary, the thyroid, and the sexual organs were present. Similar lesions were found by other observers. In 7 of the cases that have come to autopsy, lesions of the thyroid, consisting in atrophy, with compensatory hypertrophy, were noted in all; tumors of the pituitary were noted in 3 cases, with pathological lesions of the gland in 2 other cases. It would therefore appear that disturbance of function of the thyroid and pituitary bodies had much to do, if indeed they were not the causative factors, with the production of this one form of pathological fat. Interference with the sexual function has long been considered an

important factor in the production of excessive adipose tissue. Whether this is a direct or indirect relationship has not been fully determined. It would appear from the work of Froelich and others that the relationship is indirect, inasmuch as tumors of the pituitary not only inhibit sexual development, but also lead to excessive fat deposition.

In a case under the observation of one of us (McCarty), a boy when aged fourteen years, weighing less than 100 pounds, during a period of three months gained 80 pounds in weight. This was followed by mental symptoms, slow mental reaction, mental hebetude, and later, from time to time, during the last ten years, of apparent mental and physical exhaustion, with at times, delusions of persecutions. The development of the sexual function was totally inhibited, the testicle remaining the size of a filbert, with absence of hair on the pubes. In this case, in addition to the above symptoms, gigantism developed, with rapid growth, after adolescence.

We have been able to trace connecting links in several of the above groups. Beginning with adiposis dolorosa, with the predominance of thyroidal lesions, a case reported by one of us (McCarthy) in conjunction with Dercum, represents an intermediate type between adiposis dolorosa and the adiposis cerebralis of Froelich. Clinically, the case presented a combination of adiposis dolorosa and a type of adenolipomatosis of Launois and Bensaude. The patient was a man, aged thirty-nine years. Fifteen years previous, at the age of twenty-four years, he grew excessively fat, and later exhibited symmetrical deposits about the neck and trunk which were exquisitely painful to touch. He presented a marked asthenia, and for the last five years of his life suffered from major epilepsy. The testicles were undeveloped both to gross and microscopic examination; the penis was small, and there was a scanty growth, one might almost say absence, of hair on the pubis. At the autopsy a weight of 206 pounds, in a man of 4 feet 10½ inches was recorded. In this case adenocarcinoma of the pituitary body, congenital enlargement of the adrenal, telangiectatic angioma of the spleen, and acute parenchymatous nephritis were found. Extensive lymphoid infiltration was present in the subcutaneous fat, and scattered here and there numbers of hemolymph glands. In the clinical picture the presence of lymphoid material in the fat tissue in this case presents a good example of adenolipomatosis. Inasmuch, however, as the fat tissue itself exhibited both in its development and in its morphology the presence of pain and tenderness, and since asthenia and mental symptoms, all the characteristics of adiposis dolorosa existed, the case belongs in this sense to Dercum's syndrome. The rapid development of the fat after an acute infection, together with failure of development of the sexual organs, in the presence of epilepsy, with a tumor of the pituitary body, brings the case within the group of adiposis cerebralis.

In the following case a clinical diagnosis of adenolipomatosis was made. The scarcity of autopsies in this group makes the detailed study of this case of much interest from a pathological standpoint. Metatasis of a thyroidal tumor to other portions of the body, including the pituitary, makes the case well worth recording.

The history and notes of examinations are as follows:

M. McD., white, aged fifty-seven years, born in Ireland, was admitted to the nervous wards, Philadelphia General Hospital, September 2, 1906. Careful investigation of family history reveals nothing of importance as bearing on his present condition.

His previous medical history reveals intermittent fever when aged twenty-two years. Since that time he has been in good health until the present illness. He denies ever having had syphilis or other forms of venereal disease. Alcohol was used in excess for many years.

Present Illness. Present trouble began in 1903. He gave up work on account of feeling of confusion in head, with some dizziness. On attempting to get out of bed the following morning he fell to the floor. He then found that his right arm and leg were completely paralyzed. He remained in bed for a period of two months, when there was sufficient return of power in the leg to enable him to move about. Since that time there has been a progressive improvement in both the arm and the leg until at the present time he is able to use both fairly freely, with, however, marked spasticity in the right leg. On admission to the hospital there was a marked enlargement of the neck. The patient is not at all certain about the beginning of this trouble, and states that it was of slow onset and had existed for some time before the stroke. He attributed it to a gradual increase of fat, and paid little attention to it.

Physical examination shows a man above normal weight, with a marked enlargement of both sides of the neck, symmetrical in distribution, which gives to the face a bloated and frog-like appearance. This enlargement appears to be due to masses of fat tissue, freely movable, and of somewhat harder consistence than fat present in this location. There is a right inguinal hernia. The lungs show no abnormal condition. The apex of the heart is in normal position; both the pulmonary and aortic second sounds are accentuated; the heart action is somewhat irregular. The nervous examination shows the station to be fair and the gait to be hemiplegic, with marked spasticity in the right leg. The left arm is normal; the right arm is spastic, with some loss of power, the grip in the right hand being diminished. Resistance to motor tests in both arms shows a fair amount of power. The legs are fairly well developed; the right leg is somewhat rigid, and shows a marked increase of the knee jerk, ankle clonus, and a positive Babinski reflex. On the left side the reflexes are normal.

There is no Babinski reflex on the left side. The Gordon paradoxic reflex is absent on both sides. The cremasteric reflex is present on both sides. Sensation is normal over the entire body. Examination of the cranial nerves shows the pupils to be equal, with prompt reaction to light, accommodation, and convergence; extra-ocular movements are good in all directions. The right cheek is flattened. The mouth can be drawn to the right much better than to the left. Tongue is protruded in the median line without tremor. Whistling, mastication, and swallowing are performed promptly and without difficulty.

An examination nine months later, July 1, 1907, gave the following results: Measurement of the neck at the level of the thyroid cartilage is 20 inches. There is a marked distention of the veins of the neck and the upper portion of the thorax above the third rib. The veins are about the size of a goose-quill. The head is pushed forward and the neck has the appearance of downward displacement, as the second rib may be easily mistaken for the clavicle. The enlargement of the neck is bilateral and symmetrical, and is composed of isolated freely movable tumors varying in size from a chestnut to that of a small apple. These tumor masses are now firm and not tender nor painful. The physical examination of the chest shows that the expansion is practically *nil*. There is dulness to percussion anteriorly an inch to either side of the sternum above the third rib. On the left side this fuses with cardiac dulness. Posteriorly there is dulness over the upper lobes of the lungs to the midscapular region. Breath sounds are absent over the areas of dulness anteriorly. Distant vesicular breath sounds are heard over the upper lobes posteriorly. Tactile and vocal fremitus are both increased over the upper lobes posteriorly. Vocal fremitus is absent over the anterior area of dulness.

One year later (July 30, 1908), a reëxamination showed the condition to remain practically the same as that above noted on the preceding examination. The following observations, however, were recorded: There is some difficulty in swallowing; the speech is muffled and husky to such a degree that it is impossible for the most part to understand what he says. There is no dyspnea or pain. There is some limitation of movement of the head, which is more marked to the right. Dupuytren's contractures have developed in both little fingers. The blood count shows: Red blood cells, 320,000; leukocytes, 7290; hemoglobin, 75 per cent. (Fleischel). The *x*-ray examination at this time shows the heart displaced toward the right. The lungs at the apex are not diseased, but have lost their transparency to the rays, as is often seen in youth (Kassabian).

On September 4, 1908, there was a marked increase of dyspnea and the patient was removed to the infirmary. Physical examination at this time showed a marked weakness of cardiac action. There was marked loss of muscular element at the first sound,

with marked irregularity of the heart action. There were periods of tachycardia followed by periods of bradycardia. No relationship to the respiratory rhythm could be worked out. A few days later (September 10, 1908), the heart action became much weaker, with persistent tachycardia. Percussion over the anterior portion of the chest showed hyperresonance to the clavicles. Gurgling rales were heard over the larger bronchi. The patient died the following day (September 11, 1908).

The clinical diagnosis was recorded as adenolipomatosis; general arteriosclerosis; mitral regurgitation; chronic interstitial nephritis; right inguinal hernia; terminal edema of the lungs.

The Pathological Diagnosis. Malignant adenoma of thyroid, with metastasis of cervical glands; congestion and edema of lungs; cloudy swelling of myocardium, with chronic mitral valvulitis; chronic adhesive peritonitis in gall-bladder region; chronic congestion of stomach and pancreas; chronic fibrous splenitis and perisplenitis; chronic interstitial nephritis; arteriosclerosis and edema of the cerebral meninges.

The autopsy record is as follows: Body of an adult white male, about 5 feet 6 inches tall, showing a moderate fat development, particularly about the upper parts of the trunk. Muscular development fair; pupils equal, teeth poorly preserved. Neck shows the presence of a swelling which seems to be due largely to the presence of a thyroid tumor with enlarged lymph nodes of the anterior chain. Postmortem rigidity marked, lividity moderate; green discoloration of abdomen. Preliminary incision shows a moderate panniculus adiposus and pallid musculature.

Thyroid body shows marked enlargement of all three lobes particularly well marked in the lateral lobes and less so in the middle lobe. The mass is not adherent to the surrounding tissues and is easily dissected loose. The surface is coarsely nodular, and of a glistening mottled gray and green color. The consistence varies from a soft fluctuating sensation over what are apparently pea- to marble-sized cysts, to a dense firm sensation over those parts of the tumor which are the supporting fibrous elements. The cystic portions are of a green color in many places and in other places show the brown glue color so typical of colloid. The mass cuts with considerable difficulty and shows a cystic mottled cut surface from which flows a reddish-green, somewhat cloudy fluid, apparently the result of cutting through the numerous cysts containing material of the same nature. Less numerous cysts show the presence of a dark-brown homogeneous material of gelatinous consistence. The cut surface shows many heavy bands and finer fibrillæ of fibrous tissue.

Cervical lymph nodes on both sides are much enlarged; show no gross evidence of the presence of lymphoid tissue, and are apparently completely occupied by a mass similar to that found

in the thyroid body whose presence has increased the size of the individual nodes so that they measure approximately 15 x 5 or 6 mm. These are slightly adherent one to the other, but not to the surrounding tissues of the neck.

Thorax: Right pleura is smooth and glistening. No fluid in cavity.

Right lung weighs 690 grams; as it lies *in situ* it extends well over the midline and overlapping its fellow from the position of the manubrium to the level of the fifth rib; above can be seen the middle lobe of the thyroid projecting below the level of the clavicular ends; below can be seen a small triangular area of pericardium. The lung itself is voluminous, generally dark red, and shows a smooth glistening surface, cuts easily and shows a dark-red mottled cut surface from which a small amount of blood can be expressed from the upper lobe, admixed with a frothy fluid; it crepitates throughout. Bronchi are deeply injected and show slight thickening of the mucosa and adherence of a small amount of thin bloody mucus. Pulmonary artery shows a few streaks of sclerosis. The vein is normal. Peribronchial glands normal in size and deeply pigmented. The lower lobe of the lung posteriorly shows several small areas of deep color with poorly defined edges (probably hemorrhagic) and two larger areas of marked softening with a foul odor and irregular edges.

Left pleura shows dense old adhesions about the lower lobe posteriorly to the diaphragm.

Left lung weighs 1120 grams; voluminous and generally dark red in color. Pleura shows marked adhesions; over the lower lobe several punctate hemorrhages; the lobes are densely adherent. Organ cuts with ease and shows a dark-red, moist, and mottled surface from which can be expressed a large amount of frothy and salmon-colored fluid. Organ crepitates throughout. There is a small area 3 cm. in the upper lobe posteriorly where an area of consolidation is noted; this on cross-section shows a lighter color than the surrounding parts and is finely granular in appearance and shows absence of retraction in contrast to the surrounding tissue. Pulmonary vessels, bronchi, and peribronchial glands are as in the other lung.

Pericardium smooth and glistening except for an area posteriorly on the upper surface of the left ventricle where the parietal and visceral pericardium are densely adherent.

Heart is about the size of the patient's clenched fist; soft and flaccid, shows a smooth and glistening pericardium except as mentioned above. Subepicardial fat moderate in amount; muscle cuts with ease; cut surface is grayish brown in color, distinctly friable and slightly bleeding; left ventricular wall is 13 mm., left auriculoventricular orifice 11 cm., leaflets diffusely thickened, show some nodular fibrosis about the valve margins; chordæ

tendineæ show considerable adhesions and papillary apices a moderate fibrosis. Aortic orifice, 8 cm.; valve leaflets are diffusely thickened, and sinuses of Valsalva show well-marked sclerosis not involving the coronary orifices. Right ventricular wall measures, 2 mm. in thickness; right auriculoventricular orifice, 12.5 cm.; pulmonic, 7 cm.; leaflets in both normal. Ventricular cavities somewhat enlarged and show distinct flattening of columnæ carneæ. Auricular cavities normal. Coronary arteries slightly sclerosed.

Aorta: There is extensive plaque formation in aorta and thickening of intima.

Tongue basis, larynx, trachea, and esophagus normal.

Abdomen: Peritoneum smooth and glistening except the region of the gall-bladder, where there is well-marked adhesion of the liver, gall-bladder, duodenum, and colon. The ascending colon is adherent and markedly convoluted in such a fashion that the cecum lies in the right hypochondriac region with its tip about 5 cm. below the costal margin. Appendix points down and in, slightly adherent.

Spleen weighs 120 grams; shows chronic fibrous splenitis and perisplenitis.

Adrenals. Normal.

Kidneys show chronic interstitial nephritis. Bladder and ureters, normal.

Liver weighs 1460 grams; measures, 25 x 18 x 7 cm.; firm; normal shape except for a small anteroposterior fissure on upper surface. On anterior margin there is an irregular circular area 1.5 cm. in diameter, yellow colored, with a depressed centre which on cross-section is firm, resistant, and grayish yellow, hyalin in appearance, with a deeper gray depressed centre. This area is sharply defined from the surrounding tissue and apparently replaces the liver parenchyma. Organ cuts easily and shows a bulging, profusely bleeding, generally reddish-brown surface. Closer examination shows depressed red brown central areas fusing, and surrounded by a lighter, grayish-brown peripheral area.

Gall-bladder is densely adherent to surrounding parts; no marked thickening of wall; filled with cloudy, slightly thickened, viscid bile. Mucosa normal, ducts patulous.

Pancreas shows chronic congestion.

Stomach shows slight chronic hypertrophic gastritis.

Small intestine shows slight congestion and submucous hemorrhagic points, especially in the ileum.

Large intestine approximately normal. Appendix is 10 cm. in length, patulous, and except for slight adhesion is normal.

Histological examination was made of the organs indicated in the following report:

Thyroid gland (tumor): Eight sections show an irregular mass of supporting fibrous tissue, which in places is thick and shows

definite hyalinization. A lymphocytic infiltration of variable degree is noted in nearly all the sections. Vascularization is moderately rich. The epithelium for the most part is arranged in variously sized cysts, in some sections singly, occupying almost the entire area, and in others forming minute acini whose lining wall is made up of a single layer of a dozen cuboidal cells and present in almost every conceivable grade between the extremes. These cystic areas contain an eosinophilic, structureless, and homogeneous mass with edges showing some "scalloping" toward the epithelium, evidently from this and the gross appearance being colloid. The walls of the cysts show in places distinct outgrowths into the lumina of papillæ covered with the single layer of cuboidal epithelium and having a form varying from a simple finger-like projection to villi whose subdivisions and tree-like branchings are innumerable. The supporting connective tissue of these villi is slightly vascularized and loosely arranged, the cells showing moderately large vesicular nuclei. Definite penetration of the basement membrane is to be seen in only a few instances, but small collections of epithelial cells without definite arrangement and without any evidence of basement membrane are numerous and usually lie in fairly close relation to an acinus. Throughout the tumor, lying in colloid masses, in the heart of epithelial masses, in the supporting substance of the papillæ, and well out in the larger masses of hyalinized connective tissue, are moderately numerous somewhat broken, generally rounded masses of an intensely basophilic homogeneous material which has the histological appearance of a calcareous deposit. Although this is partly deposited as an irregular mass, yet there are considerable numbers of small bodies intermingled whose lamination, globular shape, and somewhat less basophilia give the typical appearance of psammoma bodies. Diagnosis: Papilliferous-cyst-adeno-psammocarcinoma of thyroid.

Cervical Lymph Node. The section shows a definitely thickened capsule, underlying which are a few lymphoid cells lying between fibrillæ of dense connective tissue. The body of the node, however, shows a mass practically identical with the primary tumor, and showing both colloid and psammoma body formation; evidently a metastasis from the primary tumor in the thyroid.

Lung: Three sections examined. The first two sections are much alike and show extending throughout almost all the section marked thinning of the alveolar walls, with rupture so as to bring about the fusion of several smaller alveoli, with the production of a larger one. Even these thinned walls show capillaries crowded with erythrocytes and an occasional leukocyte. This congestion extends throughout the section and shows itself markedly in the larger vessels of both venous and arterial type. While the emphysema is universal, many of the alveoli are filled with an exudate

consisting in many places of a dense network of fibrin enmeshing great numbers of erythrocytes, a few desquamated epithelial cells and some coal-carrying phagocytes. A moderate amount of nuclear fragmentation is present in all the alveoli. The bloodvessels and bronchi show no notable changes, except that there is well-marked dilatation of the perivascular lymph spaces about some of the larger bloodvessels. The third section of lung shows a large amount of pneumonic exudate of the same type, there being added to it a loss of outline of the alveolar walls and a fusion of the erythrocytes in the capillaries without any demonstrable nuclear fragmentation in these parts. There is also a marked edema in association with the pneumonia in this section, showing a clear structureless material taking a slightly acid stain. Occupying a position well within the consolidated mass is a generally circular, non-encapsulated mass of cuboidal epithelial cells arranged in the form of small acini from the walls of which project compound villous fibrous tissue columns supporting a single layer of the same cuboidal epithelium. On three sides small finger-like masses of epithelium not definitely papillary, push out into the lung tissue. In two places within the tumor definite psammoma bodies are seen. Several are seen lying without the well-defined zone of tumor. Diagnosis: Passive congestion and fibrinous bronchopneumonia, with metastasis of primary tumor in thyroid.

Liver: Two sections examined. The first section shows a normally thick capsule. The capsule of Glisson, however, shows a moderate fibrosis, the elements being chiefly old connective tissue with the admixture of a few lymphocytes. The parenchymatous cells show blurring of the cell outlines and slight granularity of the protoplasm. The central vein is packed with blood corpuscles, the congestion extending out into the capillaries almost to the Glissonian capsule and producing centrally considerable capillary dilatation. No definite fibrosis about the central vein. The second section of liver shows a large area made up partly of necrotic masses infiltrated with fibrous tissue poor in nuclei, these latter, however, being distinctly vesicular in type. About the central small irregular necrotic areas are grouped a few epithelioid cells followed by a somewhat thicker layer of small round cells. Throughout these layers a rich fibrous network runs. Vascularization is particularly rich penetrating well into the zone of epithelioid cells. The walls of these vessels are of about normal thickness, but examination of the arterial walls in the capsule of Glisson of neighboring parts shows distinct although moderate thickening apparently of the middle coat of the arterial walls. A section of this part of the liver was stained for tubercle bacilli after the malachite-green method of Rosenberger, with a negative result. Diagnosis: Slight perilobular fibrosis, cloudy swelling, passive congestion, and gumma of liver.

Pancreas: Chronic interstitial pancreatitis.

Spleen: Chronic interstitial splenitis, with passive congestion.

Kidney: Chronic interstitial nephritis, with arteriosclerosis.

Adrenal: Capsule considerably thickened and the vessels overlying the capsule show marked thickening of the intima. The interstitial tissue lying between the cell groups shows moderate overgrowth. A few of the circular cell groups immediately underlying the capsule show well-stained cells which, however, are apparently fused together, distinctly granular, and show more or less nuclear obscuration. The cells of the cortical chains show well-stained, sharply outlined nuclei, but the protoplasm of these cells shows markedly the presence of numerous small vacuoles. In some situations the vacuolization of the cells is not so marked, and the protoplasm shows a distinct eosinophilia. Still other cells lying somewhat centrally show the presence of fine brown granules which occupy almost the entire protoplasm and in many cases markedly obscure the nuclei. The medulla has apparently dropped out of the section so that it cannot be described. Diagnosis: Postmortem digestion of adrenal.

The pathological examination of the nervous system showed the following:

Gross examination: The pituitary body grossly is of normal size. Its posterior half is completely changed to a multiple cystic state, with trabeculæ between the cysts, and containing a colloid material, identical in color, consistence, and transparency with that of the thyroid and surrounding growths.

In the upper third of the pons there is an old thrombotic cyst, 2 mm. in diameter, just to the left of the median line, and immediately ventral to the median lemniscus. There is an extensive area of cortical softening, 4 x 2½ cm., which is scooped out to the extent of 1 cm., and affects the under surface of the occipital lobe at its extreme posterior portion. Sclerosed vessels are seen in the meninges which cover this area, intact. The cortical vessels show marked arteriosclerosis. There is no atrophy; marked passive congestion and moderate edema are present over the frontal lobe. At the base of the brain the vessels show a very extensive grade of arteriosclerosis and marked tortuosity of the vessels. Both vertebral arteries make almost a complete semicircle spreading from the medulla far out toward the cerebellum. On the left side this has produced a marked kinking of the posterior cerebellar artery. The misplaced portion of the left vertebral artery has caught the tenth nerve in such a way as to fold it. It must have influenced its function by pressure. The third nerve appears to be larger on the left side than on the right, where it is also large. The infundibulum seems to be larger than it ought to be.

The pineal gland appears to be normal. The ventricles are normal. There are multiple areas of thrombotic softening scattered

through the optic thalamus, the caudate nucleus and the lenticular nucleus. One of the areas is about 4 mm. in diameter and is directly in the internal capsule of the right side. The choroids appear to be normal. There is a slight amount of gelatinous material in the posterior horns. The cerebellum appears to be normal. The spinal cord shows a few small calcified plaques over the second lumbar segment.

MICROSCOPIC EXAMINATION. The spinal cord apart from a few cells, showing chromatolysis, shows a normal condition. A section of the cortex shows marked pigmentation of the cells of the paracentral globule and the pyramidal cells of the motor cortex. The pigment is of the yellow granular variety, somewhat similar to that seen in senile and presenile changes. The other cells of the cortex do not show this change. The basal ganglia, pons, and medulla are normal.

Pituitary Body: The microscopic examination of the pituitary body shows the general picture of adenocarcinoma. The cells are columnar in type and arranged in long acini. They have broken through the basement membrane and appear in nests of cubical and irregular type of cells. At the periphery of one of the acini, there is an accumulation of the small, irregular, neuroglia type of cell, similar to that seen in the posterior part of the gland. The acini are filled for the most part with a gelatinous material, reddish brown in color, composed of some red blood cells, hyaline material, and large plasmoid cells containing bright yellow pigment. The structure of this portion of the tumor is almost identical with that seen in the primary and secondary thyroid tumors. In the posterior portion of the pituitary body the blood sinuses are markedly distended. There are foci where the small round nuclei are so markedly distended as to give under the microscope somewhat the appearance of splenic pulp. In a reticular fat tissue surrounding the posterior portion of the pituitary body, there is an accumulation of the same type of nuclei, presenting the appearance of lymphoid infiltration, very similar to that described under hemolymph infiltration of the fat tissue in the case of adiposis dolorosa with tumor of the pituitary body.

In the reticular structure of the anterior portion of the gland, irregular concentric bodies of calcification resembling those seen in the choroid plexus, are seen.

Sections of the pneumogastric nerve show no changes.

While the diagnosis of symmetrical adenolipomatosis according to the description of Launois and Bensaude was not borne out by the autopsy, a new pathological form of fat formation was developed associated with multiple adenoma and adenocarcinoma. This term is to a certain extent a misnomer, the condition in the strict sense of the term being more of a lympholipoma than an adenolipomatosis.

The value of this case, however, is not so much in the support of a clinical syndrome of adenolipomatosis, but rather in the bearing which diseases of the pituitary and thyroid bear to the pathological fat syndrome. A compensatory reaction has been claimed and to a certain extent demonstrated between the functions of the pituitary and thyroid. No case, as far as we have been able to determine, has been placed upon record in which a simultaneous development of the same pathological process in these two organs has been found. It is impossible to determine from the lesions of these two organs as to which was primary. It may be assumed that on account of extensive involvement of the thyroid and the metastasis to the surrounding tissues, that this was the primary lesion and that the lesion to the pituitary was secondary. This could hardly be considered in the nature of a true metastasis, and would appear to us to be the result of a compensatory overaction on the part of the anterior portion of the pituitary followed by a degenerative process predetermined in its nature by an already existing similar condition in the thyroid and surrounding tissue. The relationship of diseases of the pituitary, and the thyroid to pathological fat formation has already been mentioned. This case links together three of the groups of pathological fat: The adiposis cerebralis, adiposis symmetrical lipomatosis, and adiposis dolorosa.

The adrenals in this case were normal both to gross and microscopic examination. In some cases of pituitary lesion the adrenals have been found diseased. In a case of adiposis dolorosa with adenocarcinoma of the pituitary, seen by one of us (McCarthy), marked hypertrophy of the adrenal was present.

The relation of the chromaffin system to the function of the thyroid has already received considerable mention in the literature. Not only in this case but in a series of control cases of pituitaries from other cases; chromaffin cells could be easily demonstrated in the posterior portion of the pituitary gland (McCarthy). These cells have nothing to do with the chromophil cells of the anterior portion of the pituitary. The chromaffin cells in the posterior portion of the pituitary follow the same staining reaction as this type of cell elsewhere in the chromaffin system, and more particularly in the adrenal and semilunar ganglia. The cells show their affinity for the chrome salts in a positive manner and the chromaffin granules are best seen in unstained sections after hardening with the chrome solution. The chromaffin cells in this case did not show any variation either as to size or structure or number from those in the control cases.

SOFTENING OF THE SPINAL CORD IN A SYPHILITIC AFTER AN INJECTION OF SALVARSAN.

By Leo Newmark, M.D.,

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This is mainly an anatomical supplement to a purely clinical account which Dr. Victor G. Vecki has published[1] of a young man who became paralyzed in the lower extremities after an injection of salvarsan.

Dr. Vecki relates that the patient, who was aged twenty-three years, had received at the hands of another physician from June 1 to September 3, 1908, a series of intramuscular injections of corrosive sublimate for a syphilitic roseola which had followed upon a typical indurated ulcer. On March 24, 1910, Dr. Vecki, discovering a cutaneous syphilid and extensive adenitis, treated him again with injections of bichloride of mercury. These were repeated on six successive days; then, instead of them, he was given two injections of salicylate of mercury, a week intervening between these. After this the patient did not return until May 30, 1911. It is not clear why he did come back. Dr. Vecki writes that, with the exception of swollen glands, there were no manifestations of syphilis at that time. He makes no mention of a Wassermann test. However, on June 10, at noon, 0.3 gram salvarsan was injected into each buttock. On the evening of June 12, having felt perfectly well in the intervening fifty-six hours, the man first felt a numbness in his legs, then great fatigue in them, and soon after had difficulty in urinating. Throughout the day of June 13 his condition grew worse until the power of motion in his lower extremities was almost abolished and sensibility was impaired below the level of the navel. By June 14 the paraplegia was complete in every respect.

I saw the patient with Dr. Vecki and Dr. Krotoszyner four times between June 24 and July 20, 1911. His paralysis was very flaccid. The knee jerks, at first faint and hard to elicit, after a few days became a little more active, then again sluggish, and finally, very feeble again, the presence of the right one being at first and at last quite doubtful. The heel reflex could not be obtained at any time. The plantar reflex, which at the first examination could not be provoked at all, later reappeared as an extensor response and continued so. There was no abdominal reflex. The upper border of the region of altered sensibility was irregular, tactile hypoesthesia beginning in front at about the seventh rib on the right side and on the left at the level of the umbilicus. The

[1] California State Jour. of Med., May, 1912.

dulness of sensation shaded downward into profound anesthesia. Sensibility to thermic and painful stimuli was affected up to somewhat lower levels. The patient's condition precluded an exact determination of the upward extension of the anesthesias. His bladder and rectum were completely paralyzed, he had numerous bed sores and other trophic disorders, and much fever. Neither mercury nor iodid nor an intravenous injection of 0.6 gram salvarsan had any influence on his state and he succumbed August 29, 1911.

With the assistance of Dr. W. F. Beerman the spinal cord was cut up and the sections stained in the Neuropathological Laboratory of the San Francisco Polyclinic.

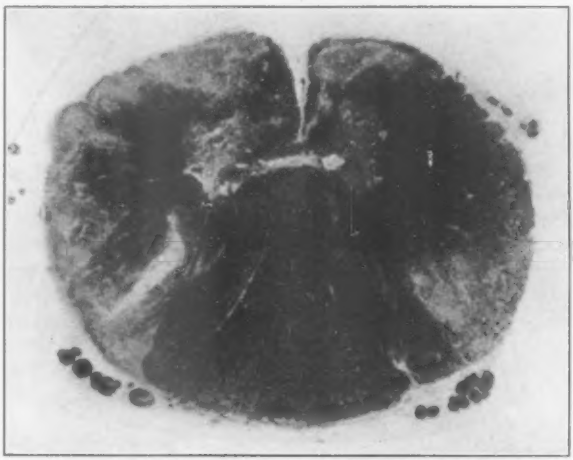

FIG. 1.—Section at upper level of softening, showing involvement of the postero-lateral region, and the anterior column on both sides, while the antero-lateral area is involved on one side only.

PATHOLOGICAL ANATOMY. Weigert's stain for the myelin sheath shows disintegration of the myelin and softening of the cord in the fourth and fifth thoracic segments. The destruction is nowhere quite symmetrical. At the upper level of the softening the postero-lateral region (containing the crossed pyramidal tracts) is affected on both sides, and so is the anterior column, but the antero-lateral area is involved only on one side (Fig. 1). Then in a section a little lower only a small area of myelin degeneration is found in the antero-lateral column of one side. This is followed by the destruction of nearly all the myelin on one side from the postero-lateral region forward to the anterior column, while on the other side of the cord the affection of the myelin is limited to

a small focus at the ventro-median corner of the anterior column (Fig. 2). At a distance of about 5 mm. below the section shown in Fig. 2, the disease becomes nearly symmetrical; ventralward from

FIG. 2.—This section shows destruction of nearly all the myelin on one side from the postero-lateral region forward.

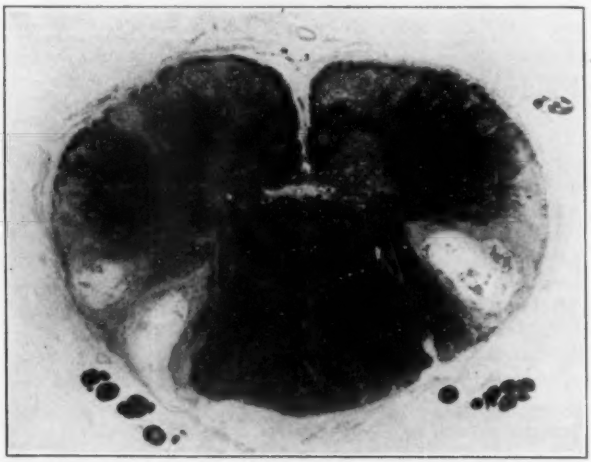

FIG. 3.—In this section of cord the disease is nearly symmetrical. In both postero-lateral areas softening has resulted in cavity formation.

the posterior horns it now spares only the white matter adjacent to the anterior horns; in both postero-lateral areas the softening of the cord has resulted in the formation of cavities (Fig. 3). Con-

tinuing the descent two small symmetrical foci of myelinic degeneration are found at the dorsal periphery of the columns of Goll next to the posterior median septum in a section which differs otherwise principally in the absence of perforations from that last described; and finally, there is a cavity again in the posterolateral region, but only one one side.

The process of breaking up of the myelin is evidently a recent one. The fragments of myelin form bodies of various sizes, ranging from large irregular masses, and drops, down to dust-like granules, either free or contained in large round cells, the granule cells.

The morbid change is more advanced in the posterolateral columns than in the anterior. The perforation of the section is not observed in the latter. The Van Gieson method enables one to trace the steps in the dissolution of the tissue. There is, for instance, a focus in one anterior column in which the disappearance of the myelin sheath is the most conspicuous result of the disease; many axis cylinders have also disappeared, those which remain are naked; the neuroglia still persists, and in its meshes is a good deal of amorphous or finely granular material. In another focus, in the opposite anterior column, the neuroglia is vanishing, one can see neuroglial fibers break off after entering the focus from the surrounding tissue. Dorsalward in the lateral columns the tissue takes less and less of the stain, large, faintly stained, round bodies (granule cells) become more numerous, there is but a trace of the neuroglia and finally this disappears in the necrosis and liquefaction of the substance of the cord in the postero-lateral region. Nowhere is any tendency to repair visible.

The gray matter shows no loss of nerve fibers. There is congestion here and there as shown by the numerous vessels engorged with blood and by occasional hemorrhages. Not only in the gray matter within the segments which show softening, but also in other parts of the cord more or less perivascular infiltration with round cells may be seen. This is also the case in the white substance, and in one place in the column of Goll, between the seventh and eighth thoracic segments, the accumulation of round cells about two capillary vessels filled with blood has assumed such proportions as to be discernible to the naked eye in the form of a speck in the mounted section (Fig. 4). This section was submitted to Professor Ophlüs, of Stanford University, and his opinion requested as to whether this formation could be regarded as a miliary gumma. He declined to apply that term to it himself, but allowed that some pathologists would probably so-call it.

The meninges are in many parts normal, or but moderately thickened, with proliferation of round cells only in a few places; but at one spot, at the lateral periphery of the cord, near an area of extreme softening the pia mater is very much thickened and infiltrated. At this place some of the dura mater is comprised

in the section, and accumulations of round cells are found in the subdural fat.

In some sections the thickened pia closes the opening into the anterior sulcus, and the pia which dips into this sulcus often exhibits proliferation of round cells.

In the softened areas of the cord, bloodvessels with more or less thickened walls may be seen, but the most conspicuous vascular changes are observed in the pia-arachnoid throughout the whole length of the cord, being by no means confined to the softened segments. There are vessels which are thickened in all their coats

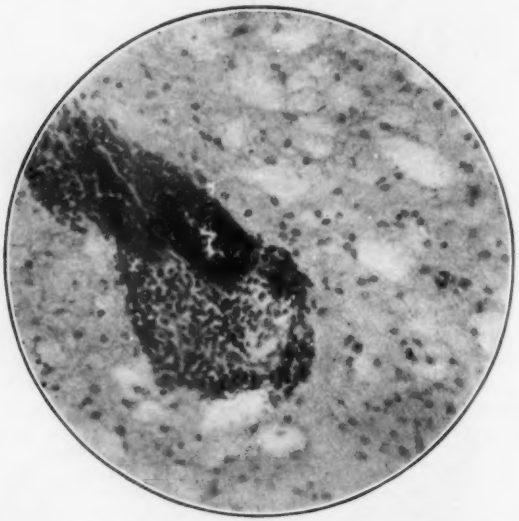

FIG. 4.—Section of cord between the seventh and eighth thoracic segments, showing accumulation of round cells about two capillary vessels.

and are completely obliterated, and now form round solid bodies of wavy connective tissue with a moderate amount of round-cell infiltration. In others the lumen is clogged by the proliferated endothelium and the wall of the vessel is thickened. In many a very small opening remains which contains blood corpuscles. The elastica of the diseased vessels does not show the resistance so often pointed out in illustrations of the syphilitic changes in arteries and veins. Weigert's elastica stain demonstrates that it is severely affected; it is distended, sometimes irregularly, or split, or broken up, and often, if at all visible, its faint fragments can be detected only when highly magnified and they remind one then of the brittle remains of worn-out rubber bands. There

is a very sharp contrast between these vessels and the numerous vessels adjoining or surrounding them which exhibit a deeply

FIG. 5.—At the bottom of this section a normal meningeal artery is shown, and above it an occluded vessel.

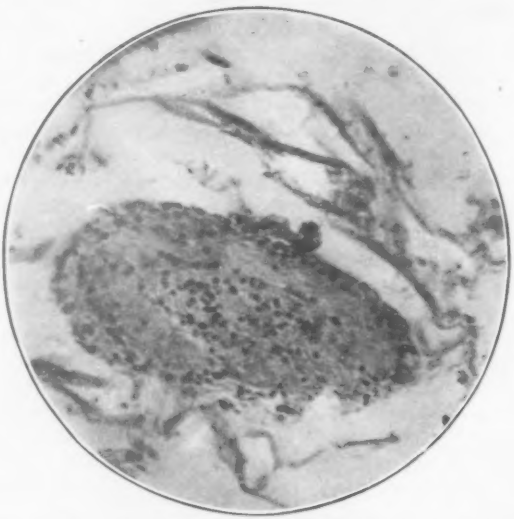

FIG. 6.—The occluded vessel seen in Fig. 5 under higher magnification.

stained normal elastica and also in other respects appear normal. These normal vessels are nearly all arteries, normal veins are far less common, and there is much reason to assume that the diseased vessels are mainly veins. Fig. 5 shows (at the bottom) a normal meningeal artery and above it an occluded vessel. Fig. 6 shows the occluded vessel under a higher magnification. The photographs are of a Van Gieson section adjacent to the Weigert section shown in Fig. 2. The vascular changes are found generally more in the dorsal part of the membranes than in that surrounding the cord on its lateral and ventral aspects, but in the lumbar region some ventral and lateral vessels are usually affected. No changes were seen in the membranes which cover the medulla oblongata.

Moderate secondary degeneration is detected by Weigert's myelin stain and also by the Marchi method in the columns of Goll and of Gowers and in the direct cerebellar tract; secondary descending degeneration in the pyramidal tracts does not appear at all in the Weigert hematoxylin sections, and in the Marchi specimens in only a very slight degree.

The gist of the foregoing is that a man who had been infected with syphilis three years before, presented the first symptoms of a fatal softening of the cord fifty-six hours after an injection of salvarsan. Was the salvarsan in any way to blame for the condition which followed its injection?

Samuel Johnson wrote more than one hundred and fifty years ago: "It is incident to physicians, I am afraid, beyond all other men to mistake subsequence for consequence." The problem of discriminating between *post hoc* and *propter hoc* continues to haunt us with all its perplexities, and in the case before us it is exemplified anew.

It is the rather close sequence of drug and disaster that impresses us with a sense of cause and effect. But opposed to the assumption of such a relation there is the clinical knowledge that acute syphilitic spinal paralysis occurred not uncommonly within three years after the infection before the introduction of salvarsan. Moreover, regarding the case from the anatomical side, it may be confidently asserted that a pathologist who might examine the specimens in this case, upon seeing the softening, the localized meningitis, the perivascular infiltration, and the widely disseminated vascular occlusions would first inquire after syphilis as an etiological factor, and, finding it, would have no occasion to seek farther. Thus clinically and anatomically the evidence in favor of the sufficiency of syphilis to produce the disease of the cord seems complete, and there would appear to be no room for the intervention of salvarsan. Even the argument which would still insist upon the striking order of events might be met, with a semblance of refutation, by an appeal to records of cases in which signs of serious damage to the central nervous system have super-

vened upon an injection of mercury. Thus a patient of Collins and Taylor,[2] who had had previously no sign of disease of the brain or cord, received one day, about six months after infection, an injection of mercury, felt the next day a numbness in the right leg, which he attributed to the injection, and at the end of a few days was paraplegic.

Of course, long use of mercury has taught us that no such effects are to be apprehended from it. But the comparatively brief experience with salvarsan has not permitted such a sense of security. A growing list of affections of the cranial nerves, the brain, or the spinal cord, subsequent to the administration of salvarsan will not let the suspicion die that we have to deal with a consequence of the remedy. Consider, for instance, the case reported by A. Westphal[3] of a tabetic woman who died seven hours after an intramuscular injection of 0.4 gram of salvarsan. The postmortem examination showed syphilitic changes in the cervical cord and in the cervical anterior roots which contain fibers of the phrenic nerve. Take, furthermore, the case reported by Juliusberg and Oppenheim[4] whose patient received two intravenous injections of salvarsan, each of 0.4 gram within six days, about three months after the infection, while the primary lesion was still present and swarming with spirochetes. Four days after the second injection this patient was seized with spastic paresis of the lower extremities, disturbance of sensibility, and complete paralysis of the bladder and rectum. As improvement ensued upon the treatment with mercury and iodid it was concluded that the disease of the cord was syphilitic.

When subsequences repeat themselves with some degree of uniformity they come to be looked upon as consequences. Hence that which with good reason might be interpreted in Dr. Vecki's case as a mere coincidence, when this case is considered by itself, assumes in conjunction with other similar observations the importance of a consequence. It must, therefore, be admitted after all that the salvarsan was somehow an agent in the final result.

The Herxheimer reaction has been adduced to explain such effects of salvarsan. The symptoms are supposed to be produced by a reaction in syphilitic tissue; syphilis seems to be indispensable for such action of salvarsan as we are considering. The drug appears to have a determining or precipitating or energizing influence upon syphilitic processes, perhaps identical with the influence upon which its remedial action depends. But there seems to be little or no reason to apprehend a direct noxious operation upon nervous tissue unaffected by syphilis. In this connection I may mention that in some cases of tumor of the brain and

[2] Amer. Jour. Med. Sci., 1909, cxxxvii, 216.
[3] Berlin. klin. Woch., 1911, xxviii, 976.
[4] Münch. med. Woch., 1911, lviii, 1558.

in the spinal canal under my observation, which owing to a misleading positive Wassermann reaction were treated with salvarsan, no deleterious results occurred, although the cases are too few to impart the confidence derivable from a larger number. Moreover, F. Epstein,[5] in the course of a discussion of the effects of salvarsan upon the eye, refers to the absence of nervous disturbances in the many patients who have been treated with salvarsan for malaria and other non-luetic diseases, and he quotes especially a report on 700 cases of frambœsia tropica in which no mention is made of any injury to the nervous system.

To Dr. D'Arcy Power, of the San Francisco Polyclinic, I am indebted for his kindness in photographing the microscopic sections.

BANTI'S DISEASE AND ALLIED CONDITIONS.

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As a result of nearly thirty years' study, Banti,[1] a Florentine pathologist, recorded his investigations in a recent paper, summarizing his conclusions, previously published in various journals, as to the nature of the disease which bears his name. This disease, though not frequent, has called forth a deal of discussion; and any one who sets out to peruse the literature is at times bewildered if not totally discouraged, as pathologists, clinicians, and surgeons are sadly at variance as to the very existence, not to speak of the nosology, etiology, pathogenesis, and pathology of the disease. At the outset it may be stated that although it seems ill-advised to include under the name of Banti's disease any case which does not conform to the tenets set down by Banti himself, the impartial critic is bound to confess that any contribution to a subject in the making, like the one under discussion, is welcome if it is made with the requisite thoroughness of observation, so that its results may count in determining the status of a disease which, to say the least, it is difficult to delimit. It is to be deplored that many of the cases which are brought to bear on this subject are incompletely recorded, and that their pathological histology has received such scant attention. Since Osler[2] first drew the attention of the profession to the subject American and English clinicians have shown interest in the disease and its allied conditions.

Banti's disease is a primary splenomegaly of unknown origin;

[5] Berlin. klin. Woch., 1911, xlviii, 2328.

[1] Folia Hæmatologica, Part I; Archiv, x, 33. See also Ziegler's Beiträge, 1898, Band iv, p. 21.

[2] Amer. Jour. Med. Sci., 1900, cxix, 54, and 1902, cxxiv, 751.

it is cryptogenetic, that is, not caused by syphilis, malaria, or leukemia. It is not a form of cirrhosis of the liver, as claimed by Naunyn, but a unique morbid entity, which shows: (1) Anemia of a characteristic though somewhat variable type; (2) cirrhosis of the liver which is identical with the ordinary Laennec's interlobular fibrous form and always is secondary to the splenomegaly; (3) ascites; (4) progressive hyposthenia, which invariably leads to a fatal issue; and (5) according to Senator[3] and Osler, it is not infrequently accompanied by severe or fatal hemorrhages from the nose, esophagus, stomach, or bowels. A low fever is sometimes observed.

In order to satisfy the practical demands of the clinician, Banti divides the disease into three stages: The first stage, which is marked by splenomegaly and anemia alone; the second stage, in which the enlarged cirrhotic liver becomes palpable; and the third, or ascitic stage. These three stages are subject to variations in length and intensity. The ascitic stage is terminal. Banti advises removal of the spleen before ascites sets in as the only means of curing this otherwise lethal constitutional affection.

What are the anatomical characteristics of Banti's disease? An extensive proliferation of the reticulum of the spleen, styled by its author fibroadenie. By this term he means to convey the fact that the lymphatic stroma of the pulp as well as that of a large number of the follicles, retains its reticular or adenomatous appearance. These changes take place primarily around the pencillated arterial system of the follicles, leaving the arterial walls intact. This pathological change is not characteristic of Banti's disease alone, but may be found in other diseases of the lymphatic system, as in leukemia. Although this process may be viewed in the light of a fibrosis, and is generally looked upon as such by pathologists, Banti lays stress on the proliferation of the lymphatic tissue of the pulp and the follicles in contradistinction to the ordinary (fibrous) proliferation of interstitial elastic or embryonal tissue. The changes in the liver are the well-known hypertrophy of the interlobular tissue, with secondary atrophy of the liver cells. Banti has taken particular pains to prove this, by probatory excisions and punctures of the liver. Naunyn[4] denies this; he claims that the hepatic changes are those of a primary lymphoid periportal infiltration. According to his view no evidence has been adduced to show that true cirrhosis of the liver develops from these interstitial changes.

Aside from the changes in the spleen and liver, there is often, though not invariably found, an endophlebitis of the splenic as well as the portal vein, at the point of entry of the former. In the

[3] Berl. klin. Woch., 1901, No. 46, and Deutsche Klinik, 1903, iii.
[4] Versammlung deutscher Naturforscher, Breslau, 1904.

third or ascitic stage of the disease, endophlebitis of the mesenteric veins is not uncommon.

It has been variously stated that Banti has classified the disease under discussion as an essential disease of the blood—as a disease of the hematopoietic organs. This is according to his own estimation of the condition, aside from the facts. Senator puts down leukopenia as a constant symptom. From the exhaustive hematological studies of Banti it is apparent that the leukopenia, though often observed, is not constant. The main blood changes are: (1) The number of erythrocytes is diminished; this is not constant, erythremia even being found in some cases; (2) the color index is lowered; (3) nucleated red cells and myelocytes are never present; (4) oligochromemia is always present; (5) leukopenia is present, though not invariably.

As regards the various forms of leukocytes: (1) There is an absolute or relative mononeucleosis; (2) there is an absolute or relative neutrophile leukopenia; (3) there is an absolute lymphocytic leukopenia.

The conclusions drawn by Banti are as follows: As the lymph nodes and bone marrow show nothing abnormal, there is on the one hand no evidence to prove that blood formation is impeded. Furthermore, as there is no urinobilinuria and no blood pigment in the spleen and the liver, there is nothing to show that there is an increased disintegration of the blood. It is, therefore, likely that the various elements of the blood are not thrown into the blood stream in sufficient quantities; there is also a possibility that they are retained in the hemopoietic organs.

What is the nosological relationship of Banti's disease in the medical system? According to Banti it belongs to the group of splenic anemias, or what is the same, primary splenomegalies of unknown etiology. He is inclined to assume two varieties of splenic anemias. The first or blood-disintegrating type of splenomegaly, in which the deleterious effect of the toxins formed in the spleen is principally exerted on the blood; in these cases the prosthenic symptoms predominate, and the patient dies from the effects of the severe anemia. In the second group, the toxins give rise to cirrhogenetic changes in the spleen and later in the liver. This latter group includes the Banti of three stages: Splenomegaly, cirrhosis of the liver, and ascites.

It should be added that in various communications aside from those of Banti, enlarged lymph nodes and embryonal bone marrow are noted, as also urinobilinuria. In his latest communication Banti states that endophlebitis of the portal root branches is not constant.

From this short review it can be seen that we are dealing here with a topic of extreme interest. This much can already be said: The various attempts to overthrow or to dissociate the pathological

and clinical complex constructed by Banti have so far been unsuccessful, and the brilliant results obtained by surgical intervention will always stand. The various points in dispute, however, call for a closer study of the subject. A great deal is still to be learned as to the etiology, pathogenesis, and delimitation of Banti's disease from apparently similar groups of diseases. The whole subject, in fact, has assumed a new phase in the light of our recent advanced means of diagnosis of syphilitic disease. In order to bring out the various points at issue, it is of advantage to pass in critical review the principal work recorded in the literature of the subject.

THE TEACHINGS OF THE NAUNYN SCHOOL. As we have seen, Banti holds that the disease is a primary affection of the spleen, with secondary implication of the liver. This is a new departure in visceral pathology, for it always has been held that, aside from certain new formations of the spleen, whatever changes are found in that organ are secondary, and are caused by inflammatory conditions of those viscera, whose blood is gathered in the portal vein. This point is specially emphasized by Naunyn, who cannot agree with Banti in the interpretation of the disease. Splenomegaly with cirrhosis of the liver (Banti's disease) is, according to Naunyn, nothing more than a cirrhosis with the precirrhotic splenic tumor of Leichtenstern. Naunyn has seen cases with considerable splenic tumefaction (30 c.c. in length), anemia, ascites, and hemorrhages which are to him nothing more than forms of cirrhosis of the liver. He would relegate Banti's disease to that class of rare cases mentioned by Senator, in which ascites supervenes the splenomegaly, without the intermediate stage of cirrhosis.

Naunyn's attitude toward the whole question is upheld by Simmonds,[5] who states unequivocally that the diagnosis of Banti's disease cannot be made anatomically. The case recorded by Simmonds does not seem to have been studied with the completeness necessary to give sufficient ground for the sweeping statement quoted above; nor does it become clear from the short report, whether this author has observed cases of true Banti's disease.

The same criticism holds good for the observations including studies in metabolism of Umber[6] and of Brugsch.[7] Umber published a case which neither clinically nor pathologically is a true Banti. Starting from the original theory of Banti that the disease is caused by some toxin generated in the spleen, Umber determined the nitrogen balance and found evidence of toxigenic proteid disintegration. Splenectomy was done, whereupon all the symptoms disappeared, and the patient made a complete recovery. The metabolism was normal shortly after the operation. To prove the value of the metabolism test as an indication for splenec-

[5] Aerztl. Verein in Hamburg, 1905.
[6] Zeitschr. f. klin. Med., 1904, Band lv.
[7] Mediz. Klinik, 1905, No. 23.

tomy, Umber cites another case with hemoglobin of only 18 per cent., which seemed absolutely hopeless; fifteen punctures were done to relieve the ascites; exitus was daily expected. The nitrogen balance being normal, splenectomy was not attempted. All at once the patient improved rapidly, the ascites disappeared, and the erythrocytes were doubled in four months; but the size of the spleen remained the same. The subsequent history not being known, this improvement cannot be considered in the light of a cure. Brugsch follows closely the teachings of the above-named authors.

The teaching of Naunyn and his pupils may be summarized as follows: There is a form of cirrhosis of the liver which is accompanied by a considerable enlargement of the spleen. The interpretation put upon these cases by Banti as a primary splenomegaly cannot be upheld. Banti's disease (splenomegaly with ascites) is an extremely rare condition, which cannot be differentiated from cirrhosis with splenic engorgement. Anatomically, the diagnosis of Banti's disease is impossible to make. Splenectomy is indicated only when the toxigenic character of the case is demonstrated by the metabolic tests. Banti's disease may recover without operative interference.

THE HEMATOLOGICAL ASPECT OF BANTI'S DISEASE, AND ITS RELATION TO THE SPLENIC ANEMIAS. Banti is reserved in the interpretation of the blood changes, as well as in its classification in the medical system; he simply states that the affection probably represents one peculiar group of primary splenomegaly. According to Grawitz[8] it may be called a splenic pseudoleukemia, as it represents a primary adenomatous proliferation of the spleen. In this connection I would like to refer to an excellent study of Hultgen[9] who has constructed a short classification of the generalized primary affections of the hematopoietic system according to their essential hematology, and subdivided them according to their etiology and clinical course. Hultgen retains the name splenic anemias, a term first introduced by Griesinger, and later employed by continental authors, Osler, and others, but discarded by Naegeli.[10] Hultgen places Banti's disease under group *a* of his splenomegalies, that is, the group of unknown etiology, while under group *b* he places the splenic anemias of known etiology, such as the malarial, syphilitic, etc. To the latter group, in my opinion, should be appended the splenomegalies due to thrombophlebitis of the portal system. The conclusions reached by Hultgen will, for the present at least, suffice to answer the theory of Banti's disease in its hematological aspect, as variously discussed by Banti, Luce,[11] Naegeli, and others. To quote: "The question as to whether in splenic anemia the plastic or the lytic function of the

[8] Klinische Pathologie des Blutes.
[9] Jour. Amer. Med. Assoc., 1911, No. 4, p. 1526.
[10] Blutkrankheiten, 1908, p. 395.
[11] Mediz. Klinik, 1910, Nos. 14 and 15.

spleen are individually or jointly involved cannot be settled as yet; but the study of blood counts of reds and total leukocytes taken from 82 cases in the literature, show distinctly parallel and synchronous movements. This I can interpret not as a sign of hematolysis, but as a slower bradyplastic hematopoiesis, as a disturbance of the entire blood-forming system."

THROMBOPHLEBITIS OF THE PORTAL AND THE SPLENIC VEINS. As noted above, Banti mentions certain inflammatory changes in the veins of the portal system as a common though not constant feature of the disease. These changes are always secondary to the splenomegaly, and as the disease advances toward the ascitic stage the portal radicals also become affected. It is evident from these statements that endophlebitis of the portal has no direct bearing upon the etiology of the splenomegaly.

Since Banti's disease has become more generally known a number of authors have described phlebosclerosis and calcification of the portal veins in its pathological and clinical relationship to Banti's disease. A close perusal of the cases so far published undoubtedly shows that in phlebosclerosis of the portal vein and its branches we are dealing with a process etiologically and anatomically different from Banti's disease. As pointed out by Borrmann,[12] it is a process much like that of luetic disease of the aorta, although traumatism is repeatedly mentioned as a contributory etiological element. In a valuable study of this subject, which also includes the experimental side of the question, Warthin[13] lays particular stress on the part played by the phlebosclerosis of the portal veins, in producing a clinical picture so nearly identical with Banti's disease. "The whole pathological picture" of phlebosclerosis of the portal veins "points to an infective thrombophlebitis," "no matter under what head reported, splenic or portal thrombosis, splenic anemia or Banti's disease." If I do not misunderstand Warthin, he identifies all three conditions, as he considers them brought about by one cause—thrombophlebitis of the portal veins. This theory cannot hold, as long as there are cases of Banti's disease reported without the detailed affections of the veins of the portal system. As already mentioned, such cases have been reported by Banti, and although it may be true, as Warthin contends, that the examination of the portal veins at autopsy is not as complete as it should be, portal-vein obstruction is accompanied by such an abundant development of the collaterals that it cannot be easily overlooked. Primary splenomegaly with cirrhosis of the liver (Banti's disease) is an entity apart from thrombophlebitis of the portal vein.

THE RELATION OF SYPHILIS TO BANTI'S DISEASE. Banti in his original communication, as well as recently, positively denies, that syphilis is a factor in the etiology of the disease in question. Within

[12] Archiv f. klin. Medizin, Band lix.

[13] International Clinics, 1910, twentieth series, p. 189.

recent years the whole subject of Banti's disease has been viewed with a great deal of interest from the fact that by reason of our improved diagnostic methods of syphilitic disease we are now enabled to substantiate the observations first made by Chiari[14] and Marchand,[15] that there is a disease which may be styled syphilitic Banti's disease, or syphilitic pseudo-Banti, which bears a remarkable relationship to the disease as originally described, both clinically and pathologically. This pseudotype is also, like the true Banti, a juvenile disease, is also characterized by enormous splenic tumefaction, enlargement of the liver, inflammatory changes of the vessels of the portal system, and blood changes similar to if not identical with those in Banti's disease—leukopenia and lymphemia. Gastric and enteric hemorrhages also occur. It is not surprising that, from the similarity of the two affections, attempts have been made to identify the syphilitic form with the original Banti's disease.

Close study of the subject reveals the fact, however, that the pathology of the cases just referred to varies materially from that of Banti's disease in the syphilitic pseudotype, the main changes in spleen and liver begin and exhaust themselves in the vascular system of the affected organs. When the process is complete, it presents the fibrous deterioration of the vessels and tissues generally which is characteristic of visceral lues. Pathologically, the syphilitic type presents a true fibrosis; a proliferation of lymphatic tissue which is characteristic of Banti's disease is not apparent. In addition to this a case of true Banti with a positive Wassermann reaction has so far at least not been observed. However that may be, the fact remains that the syphilitic pseudo-Banti bears a close relationship to the disease as described by the original author.

Anyone who studies this subject critically would be led to infer that the proof of the existence of a condition so similar to Banti's disease would tend to throw some light on the perplexing problem of the etiology of the latter; and the question naturally arises in one's mind: Has not syphilis, after all, some direct bearing upon the etiology of Banti's disease? This must not be exclusively the case, if at all; may it not, possibly, develop on the basis of a devitalized organism of hereditary or acquired luetic taint, analogous to the condition known as arteriocapillary fibrosis or that which forms the basis of certain parasyphilitic systemic diseases of the nervous system? A more complete method of diagnosis of hereditary syphilis may shed some light on this subject. Therapeutically the luetic class of cases must be viewed apart by themselves.

From the above it is evident that there is still much to be learned before we arrive at a true interpretation of the disease under discussion. No earnest effort has, so far as I can see, been made,

[14] Präg. med. Woch., 1902, No. 24.

[15] Wien. med. Woch., 1902, No. 24.

aside from the work of Banti himself, to enter into a thorough study of the histopathological basis of the disease, and we are bound to take Banti's work as the standard and accept the interpretation placed by that author upon the nature of the disease, its genesis, symptoms, and treatment. This standpoint, with certain limitations, will serve as a working basis from which the teachings of Banti can be extended. It lies in the nature of the disease, that a splenotoxic influence of the blood on the tissues, must be assumed as Banti did; to make this, however, the starting point of the whole question, has not proved satisfactory. The disturbance in metabolism noted in the thoroughly investigated case of Umber cannot be made the feature from which a differential diagnosis can be established, nor does the determination of the disturbed nitrogen balance before splenectomy bear upon the question of indication for that operation, in spite of the fact, that by this means, metabolic balance is restored. It would seem, that disturbed metabolism occurs in conditions allied to Banti's disease, and it is not unlikely, that disturbances of metabolism are but phases in the course of Banti's and similar constitutional diseases. It is safe to assume with Banti, Senator, Osler, and others, that in this disease we are dealing with a splenomegaly or splenic anemia of a peculiar type. From a broad clinical point of view it is furthermore evident, that it is above all a juvenile disease, bearing the earmarks of heredity or congenital disposition. As Luce has pointed out, it most frequently develops at the time of adolescence or shortly after, when the lymphatic structures of hereditary taint are most impressionable to various degenerative influences. With the conception of the disease, as a primary affection of the lymphatic structures of the spleen, the idea that cirrhosis of the liver is the underlying cause seems wholly improbable, although it must be granted, that clinically the differentiation of Banti's disease from certain cases of cirrhosis of the liver, with considerable splenic enlargement and severe anemia as described by Hoke[16] and Naunyn, must be difficult, if not impossible.

A careful study of the recorded cases shows that the pathological delimitation of Banti's disease from other forms of splenomegaly and from apparently identical conditions, always assuming the Banti standard, is practicable. The Gaucher[17] type of splenomegaly is a distinct entity; considerable confusion is shown in the literature by confounding the two conditions. It should be stated here that there are certain carefully observed cases still unclassified which bear a relationship to the Gaucher type, and which have nothing in common with true Banti's disease.

In conclusion, the following may be said: Banti has formulated

[16] Präg. med. Woch., 1899, Band xxiv, p. 451, and 1901, Band xxvi, p. 481.

[17] A. Borissowa, Virchow's Arch., 1903, Band clxxii, p. 108, and Stengel, Amer. Jour. Med. Sci., 1904, clxxiii, 497.

one group of splenomegalies, that which now bears his name, leaving for further research the grouping of other splenomegalies. The important factor of etiology he has left open. It is clearly the duty of other observers not to attempt to dissociate his symptom complex, nor to designate an allied symptom complex as Banti's disease, which differs intrinsically from that described by Banti.

THE CLINICAL ASPECT OF BANTI'S DISEASE. It is not the intention of the writer to discuss the differential diagnosis of Banti's disease from its allied conditions. The reader is referred to the excellent treatise by R. Hutchison and J. C. Ledingham,[18] for a summary clinical picture of the splenic anemias. Brill[19] holds that the Gaucher type can be distinguished clinically from other types or groups.

What seems most important to me is that for clinical purposes it is at present possible, first and foremost, to divide the splenic anemias into two groups: (1) The group with the positive Wassermann reaction, and (2) the group with the negative Wassermann reaction.[20] This classification will *eo ipso* determine the course of treatment, not losing sight of the fact that the Wassermann reaction may prove negative in cases of syphilis. I would propose that a provocative salvarsan injection (intravenous) be made in every case. Repeated treatment with salvarsan, together with the old-style energetic antispecific treatment, will always be in order as a tentative measure, especially in view of the fact that a certain group of cases is undoubtedly due to lues congenita tarda. Not too much, however, should be expected from the antiluetic treatment, as the disease, as shown by the fibrous organic changes, has already passed into the parasyphilitic stage, which is only in part (if at all) amenable to treatment and cure by means of the remedies at present at our command.

Finally, it should be stated that splenectomy has yielded excellent results,[21] and that the third or ascitic stage of the disease may now be successfully treated by the combination of splenectomy and the Talma operation. Altogether it is no exaggeration to state that the work of Banti stands today as one of the most brilliant achievements of medical science.

[18] Splenic Anemias in Allbutt and Rolleston's System of Medicine, v, 757.

[19] Medical Record, March 2, 1912, p. 444.

[20] Neuberg, Zeitschr. f. klin. Med., 1911, p. 92, and Ridder, Charité Annalen, 35 Jahrgang, p. 193.

[21] According to Rehling, 8 per cent. mortality in 70 cases; see Festschrift des deutscher Hospitals, New York, 1909, p. 320. Rehling transfused before operation.

CASES OF JUVENILE PSYCHASTHENIA: TO ILLUSTRATE SUCCESSFUL TREATMENT.[1]

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Definition. The conception which Janet has formed of psychasthenia is described by him in so masterly a manner as "mental uneasiness, a state of disquiet, feelings of incompleteness, without anatomical lesions." These are interpreted by him as due to the diminution of "psychological tension." Hence, the superior functions of the brain, those of correct associations of ideas and emotions, are replaced by such inferior activities as motor impulsions, such as tics, dromomania, and other motor agitations; emotionally by distress (angoisse) and morbid fears (phobias); and intellectually by mental ruminations and manias. It is the interpretation of this state by the patient of intellectual type which leads to more systematized obsessions, which it is useless to attack directly by persuasion, for they represent a much more profound cause of which they are only a last expression. Janet recognizes the likeness of this condition to that found in cerebral "neurasthenia" of the classic type and some kinds of paranoia. There are certain resemblances also to epilepsy and hysteria. He thinks the psychasthenia may be due to an intoxication or congestion, varying with the influence of infectious diseases, fatigues, and emotions in accordance with a predisposing heredity.

The syndrome which Janet calls psychasthenia had often been noticed previously and described under such names as cerebral neurasthenia, phrenasthenia, disequilibrated degeneracy, and monomania. Janet's great merit is to have shown the essential identity between manifestations which appear so different. For example, he has shown that agorophobia and claustrophobia are really two variants of a state of fear which has become morbid by being inopportune and out of harmony with reality; furthermore, the states of phobia, or angst, are merely two of the manifestations which the same patient may show when suffering from psychasthenia. Motor impulsions, of which the tics are a striking example, are merely another way in which is expressed the fundamental state of "incompleteness."

In some patients neither emotional nor motor symptoms are conspicuous; but the asthenia of the psyché reveals itself by a state of intellectual doubt, by need for verification of minute details, indecision, and a feeling of difficulty in arriving at certitude regarding the reality of anything. Janet considers the last the

[1] Read in the Pediatric Section, Amer. Med. Assoc., Atlantic City, June, 1912.

cardinal symptom of psychasthenia, and calls it "the loss of the function of the real." Naturally, this leads to a longing for moral support, comfort, and affection, and entails a fear of being alone, or in extreme cases, sometimes the moral distress leads the patient to relieve it by artificial excitants. Work and pleasure may be employed; but too often nepenthe is sought in narcotic drugs or debauch.

PSYCHASTHENIA IN CHILDREN. The full syndrome is only possible in people of complex intellect with highly developed emotions. Hence, children can hardly show it completely. Janet, moreover, studied psychasthenia in children only retrospectively through the reminiscences of his many patients. Although he himself indicates the conditions in childhood which favor the psychasthenic state, he has not unravelled its genesis so completely as have more recent analysts of psychoneurotic persons.

All agree that the scrupulosity and over-conscientiousness which mark the psychasthenic character are the result of over-strict training ill-adapted to the need for untrammeled unfolding required for a child's proper development. The moral and religious sanctions which appeal to the adult are injurious to this development, unless they are specially adapted to a child's intelligence and needs.

This opinion, although well founded, is based upon wide observation rather than upon individual analysis of children; for I know of no psycho-analyses of young children by trained men, with the exception of one made on a five-year-old boy by Freud, which is vitiated as an experiment because the boy's mother had been analyzed by Freud and was herself permeated with his ideas, so that it is impossible to exclude the influence of these upon her child.

Thus it is particularly gratifying to be able to bring forward some observations on psychasthenic children whom I had the opportunity of analyzing. More especially is this satisfactory because recovery was obtained in each case, and best of all, this occurred without the enormous expenditure of time which is believed to be essential for reaching the curative point in a psycho-analysis. Working against time to catch a train, three-quarters of an hour sufficed in the first case, and not more than an hour was consumed in the examination of the second case. In both cases, however, the history had been previously obtained. The third case, in an older child, more complex, although not completely analyzed, was cured as a result of four interviews which averaged less than an hour each. This economy of time is only possible to one who is experienced in the technique and psychopathological data, so that he may not be led by false scents to explore by-paths without practical significance. When this capacity is attained, the method can be employed in private practice; and even dispensaries should not

be deprived of its advantages,[2] for there are few procedures of practical medicine in which the direct benefits are of greater value than in the restoration to economic and social capacity of the suffering psychoneurotic, who is not only a sufferer himself, but a burden to all his connections.[3]

TICS FROM MONOMANIA. CASE I.—A girl, aged eight years, an only child, was sent to a Washington sanatorium because of numerous grimaces and gestures. These led her attendants to believe she suffered from chorea, to give her large doses of arsenic, and to isolate her from her friends, while overfeeding her. At the end of a month she returned to the country, the morbid movements having ceased, but she suffered from insomnia and was unable to go to school, in the belief of the parents, because of her "nervousness," which was especially conspicuous when reading and studying was required. When she was nine years old I was asked to see her by her uncle, Dr. Perry, of Lyons Creek, Maryland, in the hope that something further could be done.

I found a well-nourished, self-contained, sensible child, without apparent shyness, overforwardness, or hyperexcitability; but she was apt to talk rather fast, and stammered now and then. I soon discovered that she was fond of play and the companionship of which she had been deprived, to compensate for which she made believe that the objects and persons of her play were real. So rigorously was she protected that the conceptions of lying and stealing were hardly clear to her. She had been strictly managed, scolded, and repressed a good deal. She was once whipped for persistent dawdling on her way home from school. She did not remember other corporal punishments. Her life, however, was not felt to be unhappy; for she was very obedient, and was not galled by the good manners expected of her. However, she wanted to grow up, hated people to call her little, and disliked the spoiling which was a tendency of her father before her sickness. Although she did not repine at staying from school, she wished to learn to read and write; but as lessons agitated and kept her awake, she employed herself in play.

The source of the movements she had made was revealed after some hesitancy. It seemed that her mother had taught her, when aged about five years, that people lived by inspiring the air and what they expired was hurtful. This thought led to a distressing compunction about the noxiousness of her breath; if it was bad it must hurt others.

Now her training had been such that to hurt others was a great offense; but not to breathe was to die. Out of this dilemma she

[2] See author's "Care of the Mentally Disturbed," New York Med. Jour., September 29, 1912, in which is described the organization of such a hospital and dispensary.

[3] The basic principles upon which are founded the methods of management of cases of this kind were first set forth in the author's "Psychotherapeutics: A Symposium," in 1909, in the chapter on "Psychoprophylaxis in Childhood;" also in Jour. Abnormal Psychol., June, 1909.

found a way. Hurts could be mended; when injured did not some one "kiss it better"? Could not she then kiss better her own bad breath so that it would not injure others? Accordingly she made movements of her lips, which represented the healing kiss to ward off the danger of the deadly air she expired.

Later on her discontent was augmented by scruples against the injury she did by walking upon creatures with the hard and sharp heels of her shoes. Even the planks of the floor were of the animated world, which it was wrong to destroy or injure. To assuage the distressing thought of this, compensation must be made. She found it in another legendary therapeutic procedure, the healing touch. So it became her habit, before walking over an object, to bend and touch it with her hand.

These procedures belong to the class of mental manias which Janet has called manias of expiation. In their motorial character they approach the tics, into which they gradually blend. That they had done so to some extent in this case is shown by the fact that the kissing nature of the lip movements had not been suspected.

That the movements had not developed entirely into mere symbolic vestiges of their original purpose was due to their arrest comparatively early. That they would have developed into characteristic tics[4] is confirmed by the distress the child suffered in overcoming them. She did so after being in the sanatorium a few days, and did it deliberately and by a hard struggle, because she wished to return home, and they had promised that she could do so if the movements ceased. It is possible that the nurse who said this had an inkling into the psychological character of the child's disorder. After she succeeded, the desire to repeat the movements quickly ceased, although she does not know that she was enlightened regarding her notions about the hurtfulness of expired air and hard heels.

Proceeding to the genesis of the insomnia and difficulty in reading and study, interrogation showed a simple mechanism. Apprehension as to their consequences was raised in the child by the attitude of the parents, whose open fear lest they should perturb the child reminded me of the procedure of the mother of the boy whose hysterical hydrophobia was precipitated by her sitting by his bed reading about rabies two weeks after he had been bitten by a supposedly mad dog.[5] So in this case the ostentation of their solicitude provoked in the child that which they feared.

TREATMENT. The explanation of these mechanisms to both parent and child was the first task, and it proved simple, for they were intelligent people. The corollary that the child was not

[4] The nature and diagnosis of tic is discussed by the author in the Southern Medical Journal, August, 1909; Monthly Cyclopedia, January, 1910; International Journal of Surgery, August, 1910.

[5] Miller, Jour. Abnor. Psy., 1910.

morbid except by induction was then set forth. The conclusion was that the child should resume study and return to school in the fall in every respect like an ordinary child, now that the mother and father were warned against the evil consequences of unwise solicitude, and the induction of hyperconscientiousness in matters beyond the intelligence of a young child. The result has justified expectations, the child taking part in the school life with enjoyment.

Some might explain the case as a "fear wish" reaction of the ædipus type in relation to father and mother. Indeed, to the exponents of the theory upon which it depends the patient's history is not without significance, and in the absence of a dream analysis they cannot be satisfied in rebuttal. The fact, however, rests that a painful complex originating at least by the fifth year had resulted in psychogenetic symptoms, and this complex depended upon a moral concept in which the sexual life seemed to play no part whatever.

This plain mechanism of fear of bodily harm from without seems to be a much more fundamental feeling, if one is to appeal to phylogeny, than is that concerning the relations with others termed sexual. Even hedonic affects occurring autochthonously in childhood, although of the same genus as that which later effloresces into sexual emotivity, do not by any means in themselves give origin to perturbations of the psyché either in childhood or later. I say in themselves, for I believe that the perverted affectivity from which arise so many obsessions, phobias, etc., is always the product of induction, if not directly and naively from without, at least by logical induction from data acquired by observation or didaction of the conventions of family and social life. The child's avidity to relate himself correctly to these, to behave as a grown up, that being of marvelous privileges, is not sufficiently realized. It makes him seize upon the most trifling detail for imitation. One of his objects is to transcend the amusement he provokes in trying. The shame he feels at the ridicule with which his attempts are so often met causes him to keep them to himself in half shame.

Case II.—Thus in a case of which the analysis occupied over a year, and would accordingly take too long to recount, the obsessions, which were mainly sexual scruples fundamentally, had as their basis the moral and religious repressions of the patient's childhood. It was the horror and loathing of everything pertaining to the corporeal which caused the child, when aged six years, to look upon a hedonic state which used then to occur as a sinful one, which prevented even speaking of it to the mother, and which was the incentive for the repression of indulgences demanded by a most affectionate nature, for in the family all display of affection was discountenanced. It was the lurking fear of that which was awful, because unfaced and vague, but which contained inexplicable potentialities for evil, which later permeated

the patient's relations with fellow-beings to a degree which produced utter incapacity for daily life.

PREPUBERAL IMPULSIONS. CASE III.—Let me ask you to contrast on the one hand the loss of a quarter of a century of fruitful activity by this patient, the lack of good sense in whose upbringing was so late compensated for by what we have learned of psychopathology: with the immediate compensation of an entirely similar syndrome in a clergyman's child, aged ten years, whom I saw recently. One day she would be well and the next crying, feeling miserable, tired, and dizzy, with a dull headache as a result of lying in bed thinking. The preceding summer at school she had been irritable, cross, impatient, and quarrelsome with her sister. She had formerly been easy to manage and full of life and joy. Her mother was most anxious, and took pains to avoid startling or fatiguing her, and in the belief that it exhausted the child, forbade the impulsive squeezing and kissing which the child frequently desired. She had noticed that the little girl was less impulsive and irritable when having something to do, but she had been taken from school, which seemed to aggravate her nervousness.

The physical examination was negative, with the exception of a slight hyperopic astigmia and a variable visual acuity without apparent cause (Dr. F. N. Chisholm, who referred her).

Psychically, intelligence was normal. She was timid, hyperconscientious, and much concerned at having been reproved for impulsive shouting, for violent hugging of her parents, and because of some eau de cologne she took. This had really been taken by the little sister, who was punished for it. She was sometimes so unhappy and miserable that she did not want other children near her, and she was most unhappy because she was not allowed to show her affection for her father and mother, of whom she is very fond, more especially of the latter. Her dreams are rare, but she recollected one of a white-bearded man who dragged her from the bed by her hair and another of a wild animal trying to eat her. I could not at the time obtain any associations from either of these, and, indeed, I was more concerned relieving without delay the intensity of the repressions which made the child's life a burden.

A physical factor complicated the case, the child eating excessively of meats and oatmeal, and making her principal meal at night. I believed this was the initial cause[6] of the irritability of temper and the impulsiveness which led the overconscientious parents to repress overmuch.

TREATMENT. Mid-day dinner was prescribed, and a supper mainly of carbohydrates and fruit, after which she should not go to bed for at least an hour. On waking in the morning the child

[6] See author's "Diet in Nervous Disorders," New York Med. Jour., April 6, 1912; Canada Public Health Journal, June, 1912.

was instructed to make a practice of getting up and going outside instead of ruminating in bed. The parents were told to avoid nagging her about trifles, and her behavior was to be left to take care of itself at present. Her affections were to be indulged and reciprocated; she was given plenty to do, and was sent back to school in a few days. This policy resulted in complete recovery within two weeks, the child being as happy and joyous as she formerly was.

Diagnosis. I considered this a prepuberal emotionalism attributable to an incorrect dietary and greatly aggravated by parental interference, well meant but entirely injudicious. This last, the psychogenetic factor of the situation, was the main pathogen of a state which might have eventually attained a gravity like that of the case with which it contrasts.

Thus the psychasthenia of this little girl was cut short long before its root branched into mental manias or before there was a hint of obsessions or phobias. It may astonish one that I include this case in the psychasthenia of Janet, as it is without the stigmata or cardinal symptoms of that disorder, if we except the impulsiveness and the inadequacy which were hardly even conscious. The justification of such a diagnosis need not, however, detain us, for it has been set forth in explanation of the case of a child, aged only two years, which I reported to the Psychological Society of Paris in 1910.[7]

Multiple Manias of Expiation. Case IV.—However, in the following case the psychasthenic syndrome was in full efflorescence:

A boy, aged thirteen years, was referred by Dr. Guy Latimer, of Hyattesville, Md., because of extreme timidity, many "nervous" tricks, and an inability to concentrate his attention. The most conspicuous symptoms were an arithmomania, a mania for verification, including a "délire de toucher" and a "manie du sort," one of the forms of which was the imperative need of lying on his back on the floor at frequent intervals while dressing in the morning. These various mannerisms intermitted and replaced one another.

Analysis revealed that all were in reality expiatory penances for a jealousy of his little brother, which had already begun at the age of three years, when he asked that the baby be thrown from the window, and once banged his head on the floor while enraged. He himself had always been much petted, and he craved it. It was the reproval of an aunt which first created the shame for his jealousy and led him to make penance in these fashions. Latterly, he had been urged to cease his peculiarities, and can stop any of them when on the alert by a hard struggle. His distress at doing so, moreover, soon passes away. But his frequent absence of mind in day dreams, which he loves, interferes with his endeavors. This tendency was favored by his not having been allowed to play the

[7] See also Arch. of Pediat., 1910.

games of which he is fond with the boys in the neighborhood, which is a rather rough one.

This desire for expiation began when he was aged between three and four years, by thinking it was mean not to give his toys away and so he gave them all to his brother. He was told that it was naughty to be jealous, and he felt ashamed, but did not cry, but just sank into himself and said nothing. He still reproached himself. If his mother did not pet him for a week he thought she did not care for him, and so he would be unhappy.

He does not know the reason why he is jealous of his brother, for he loves him, and they do not quarrel much, even when the other cheats at play. It is in the morning and at night that he is most beset by his manias, and he feels things would go wrong night or day if he did not perform them. He declares: "I always seem to want to do something I do not want to, because I do not want to." He does not know why. He has no shame of body or sex, as he has been fully instructed. He is very religious, believing in heaven and hell, that he must be good, and feels that he ought to make himself sad because he does not like to be sad; but he is so prone to sadness that even as a baby music made him cry. So conscientious is he that he undertakes every task with too great violence, quickly becomes exhausted, and then has to fight against the dreamy tendency which supervenes.

TREATMENT. Having explained together the genesis of his desire for penance, we decided to concentrate attention upon only one of his manias at a time, in order to break one by one the habits he had formed, and he was to take up carpentry work in order to combat the tendency to day-dreaming. His diet was also rectified.

More and more control was soon obtained. On last hearing from him, a year later, he had taken a position, and had overcome his disabilities.

The psychogenetic factor in this case was obviously the unwise manner in which an affectionate infant's natural jealousy was reproved by over-religious relatives. The awfulness of the sin fostered the poor boy's shame thereat, and led him to the type of expiation which follows from a misapplied asceticism.

GENETIC TYPES OF PSYCHASTHENIA: RELATION TO HYSTERIA, ETC. Thus in its essence psychasthenia arises as a reaction of discomfort and anguish against unnatural repressions. It is psychogenic in this form; but there is perhaps another type which precedes from a general uneasiness of the body due to a toxic factor.

CASE V.—Such was the case of a child, aged two years, whom I saw in the dispensary at the Children's Hospital, of Washington, with Dr. Donally. Distressing howling without relation to extraneous stimuli, the eating of sand and clay, the maintaining of a large deep sore on the wrist by scratching were among the chief symptoms which betrayed her general discomfort, against which these were

morbid reactions. I interpreted them as due to what would have been shown in older people by a sentiment of incompleteness. The cause was believed to be a diet almost exclusively of strong coffee and milk since the age of three months. The case was reported in full to the Society of Psychology of Paris, and was published in *Pediatrics*, 1910.

A Symptom which is Usually Psychoasthenic is Stammering. Case VI.—The ten-year-old son of a Washington attorney was referred in November, 1910, by Dr. Spiller, of Philadelphia, for advice regarding a stammer of two years' duration and for "general nervousness."

A brother who had formerly stammered at the same age had recovered after six months spontaneously; but the expectations of the parents that this boy's stammer also would disappear were not fulfilled. He stammered worse when tired or when intent upon speaking correctly. In play, he rarely stammered, and a sentence was never interrupted by a stammer. The boy was fidgety, especially on speaking; but his writing was not jerky. His attention was easily tired. He was not overstudious. He did not tremble. He was not constipated. He detected differences of pitch.

His chest was contracted in front, and measured during quiet speaking twenty-three and one-half inches, expanding to twenty-four and one-half inches. By forced inspiration it could reach twenty-nine and one-quarter inches. In singing he expanded to twenty-seven and one-quarter inches. The scaphoid scapula was not present.

I omit the detailed psychic examination for the sake of brevity. In short, the cause of the stammer was a common one, the dread lest he should stammer, added to or supplemented by an insufficient preliminary inspiration. The attempt to force the voice to overcome these difficulties only added to the glottic spasm, and the contortion of the muscles of forced expiration due to his apprehension.

A series of exercises in control led to his recovery in a few months. Now the treatment of this boy succeeded only by virtue of taking into due account the psychoasthenic factor in the production of his stammer; and while that was attended to, the boy remained well for several months. When a few months ago this was neglected a relapse occurred.

The fact that a disorder may be psychogenic does not identify it with hysteria, the psychogenic disorder *par excellence*. There is still much difference of opinion how we shall define hysteria; but as I see it, the essential character of the disorder is that it is induced by an idea. This may be either revived from the patient's mind by an occurrence which strikes an associating idea or it may be direct by what is regarded as suggestion. The mechanism is the same in each case, and the term suggestion is appropriate for both.[8]

[8] See Nature of Hysteria, Int. Clin., 1908, iii; also Amer. Jour. Med. Sci., August, 1910.

The induction which results in psychasthenia, unlike that in hysteria, is indirect. The patients indeed are not suggestible, and cannot be hypnotized as can hystericals. What is induced is a general state of ashamedness, timidity, and scruple; and it is from this morbid root which spring, by psychological processes entirely natural, the train of ruminations, anxieties, morbid fears, and manias to touch, to count, to search the past or future, to explain, to verify, and repeat, to attain perfection, and the mysticism which springs from this desire. The mania to compensate, to expiate, and to make compacts with Fate, too, proceed from a feeling of unworthiness which a scrupulous person has. From this root spring also the morbid fears of objects, of situations, even of one's own thoughts and bodily functions. The anxiety neurosis is simply one of the ways in which is manifested the psychasthenic state. A full discussion of the reason for the belief in disagreement with Freud is given by Janet, but would take too long to recapitulate.

The relation of psychasthenia to tic has been indicated above. The impulsion to tic is derived from the general discomfort and nervous instability being focussed by peripheral or central irritation upon some particular part of the body or upon some action. One type of occupational dyskinesis is an interference with the action desired through an impulsive tic which takes possession of the muscles needed for the desired act. In the author's[9] studies of writer's and telegrapher's cramps, this is discussed at greater length.

Finally, neurasthenia must be considered. I am of those who believe it advisable to cease the use of this term, or at least to restrict it entirely to cases of abnormal fatiguability which is not induced by an idea nor caused by infections or toxines, disorders of metabolism or perturbations of the internal secretions. It is certain that psychasthenic symptoms appear quite apart from fatigue, which psychasthenics can sometimes support for long periods. Hence the treatment of the disease by extranutrition, rest, or any physical procedures is in psychogenic cases both superfluous and harmful, in that it detracts attention from the real source, namely, the psyché of the patient.

For Correct Treatment. Proper knowledge of the constitution of the mind of the child is the only foundation upon which to build this successful therapeusis. The diagnosis into categories, such as hysteria, neurasthenia, phobia, monomania, followed by an empirical treatment, is utterly useless because not accompanied by adequate notions of the process occurring in the mind of the patient. Doctors who treat neurotic persons with such inadequate equipment will meet with even less success than do the followers

[9] Jour. Psych. u. Neurol., Leipsig, May, 1912; see also Jour. Abnorm. Psych., June-September, 1912.

of an unlicensed cult; for these have a conception, however erroneous, of psychological mechanisms, and it is a conception which happens to fit a certain proportion of cases, whereas the usual physician's conception fits none at all. And a neurotic who gets well under his care does so not because of his medical treatment.

Now psychological mechanisms are most pure, and hence most easily understood in children; and it is in order to appeal to pediatrists and physicians for proper study of the nervous children they see that I bring before the profession the foregoing considerations.

I should like to add that one of the reasons why pediatrists do not take more interest in neurotic children is because the books generally take this subject up in such an unsatisfactory, vague manner. Epithets rather than causal mechanisms seem their aim. My paper is an attempt to show some mechanisms at work in individual children. The analysis and therapy do not require any special ability, merely a serious study of the child's usual and unusual modes of thought. Most of us can study this upon our own children. Besides, the analysis is easier than in the adult, for a child has less complicated motives for concealments.

Psychic disorders should be observed and analyzed clinically by a scientific method essentially similar to that used in all clinical and experimental medicine. Loose general terms have no diagnostic value until conceived with definite meaning. Such an *olla podrida* as "neurasthenia" must be either restricted or abolished if progress is desired.

Of the cognomen hysteria the same may be said, unless the term is used in a definite sense like that of Babinski, "any symptom producible by suggestion." The lesson of my cases is not the cognominal diagnosis, psychasthenia, but the revelation of the mechanism of each separately, and its removal by rational measures very different from those found in any text-book of pediatrics or even neurology.

THE INCIDENCE OF PURPURA IN THE COURSE OF CHRONIC PULMONARY TUBERCULOSIS.

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Purpura was known to the ancients, but under this name they not only included the hemorrhages into the skin but also the

eruption of scarlet fever and measles. In 1694, Zeller, Professor of Medicine in Tübingen, gave a good description of purpura. Werlhof described it under the name of morbus maculosus, and finally, Schönlein gave it the name of peliosis, in describing what he thought was a distinct clinical entity. Rayer, in 1827, was the first to publish a case of purpura associated with tuberculosis. Louis, in 1843, mentions a tuberculous woman, who a few days before her death showed bluish spots. Since then there have been numerous other contributions to the literature on the subject.

Bensaude and Rivet,[1] however, in 1906, after a study of their own cases during ten years and of the cases reported in literature, have written so far the most complete monograph. They classify the cases from a clinical point of view in four categories: (1) The cases of purpura hæmorrhagica occurring in the course of miliary tuberculosis. (2) The cases of purpura hæmorrhagica occurring in the course of chronic pulmonary tuberculosis. (3) The cases of purpura hæmorrhagica occurring in the course of latent tuberculosis. (4) The cases of purpura hæmorrhagica occurring in the course of some extrapulmonary tuberculosis. In discussing the cases occurring in the course of miliary tuberculosis they say that all the cases reported in literature that have come to autopsy show that they were not caused by a primary acute miliary tuberculosis, but by an acute miliary tuberculosis occurring in the course of a chronic pulmonary tuberculosis. They themselves have never had the opportunity to observe a fatal case of purpura occurring in the course of miliary tuberculosis.

According to these authors, purpura occurring in the course of undoubted chronic pulmonary tuberculosis is much more frequent, and most commonly appears in the terminal or cachectic stage of the disease. Its most usual form is the simple purpura, the so-called cachectic purpura, but often one sees a true purpura hæmorrhagica.

They say that there is a purpura that is premonitory of tuberculosis, upon which Rendu insisted in 1890. According to Rendu a purpura situated on the dorsal region of the hands and wrists is quite a pathognomonic sign of a latent tuberculosis, especially in old persons. There is also a true pretubercular purpura hæmorrhagica, as is well shown in the case reported by Carnot, Bensaude, and Harvier:[2] A young woman, weakened by childbirth, and nursing for six months, grew thin for three weeks. She was then seized with a serious purpura, having multiple hemorrhages from the nose and gums accompanied by hematuria. These symptoms continued for three weeks until she was in an extremely anemic condition, and there were grave fears for her life. The hemorrhages, however, ceased and her general condition improved rapidly.

[1] Presse Méd., 1906, xiv, 469.

[2] Bull. Soc. des Hôp., 1906, xxiii, 375.

Although numerous examinations of the chest were made it was not until fifteen days after the disappearance of the purpura that any evident signs of pulmonary tuberculosis could be found. Tubercle bacilli were found in the sputum and urine. The tuberculosis, without any other signs of purpura, advanced rapidly to cavity formation in six weeks.

There are numerous cases of purpura developing in individuals suffering with extrapulmonary tuberculosis. Gossner[3] reported a case of a man with a tuberculous testicle who had three repeated attacks of purpura before castration was performed, after which he had no further attacks of purpura. Coley and Ewing[4] have reported a fatal case of purpura hæmorrhagica occurring in the course of an acute lymphatic tuberculosis. There are also other instances reported in literature of purpura complicating chronic pleurisy, peritonitis, tuberculous adenitis, tuberculous cerebrospinal meningitis, etc.

Bensaude and Rivet think that purpura is not infrequently associated with tuberculosis. Of their 35 cases of chronic purpura hæmorrhagica, 7 occurred in individuals undoubtedly tuberculous and 5 in individuals probably tuberculous. They say that in the presence of a purpura, particularly in the recurring or chronic form, when the cause is not apparent, the clinician should, by all means in his power, look for some chronic tuberculous lesion either of the lungs, or of the glands or of some other portion of the body. Brown says that purpura hæmorrhagica rarely occurs in tuberculosis. In the last 1000 cases at the Adirondack Cottage Sanitarium but 3 cases have occurred. This corresponds very closely to my figures. Out of 1626 ward patients at the Phipps Institute, I was able to find only 8 cases of purpura. Mackenzie, in 200 cases of purpura, found it associated with tuberculosis 4 times. Pratt,[5] in 258 cases of purpura, both primary and secondary, found it associated with tuberculosis 7 times.

The pathogenesis of purpura is still an undecided question. Weichell thought that the purpura was caused by the absorption of toxins from a rapidly breaking-down tuberculous area. Some of the writers have been inclined to lay the cause to a secondary infection, such as the case reported by Widal and Thérèse in which the blood and different organs contained streptococci. This finding, according to the different investigators has been rare. Others have favored the tubercle bacillus as the direct cause, since it has been clearly demonstrated by Jousset,[6] Rosenberger,[7] and others that the tubercle bacillus can be found in the circulating blood of both acute and chronic tuberculosis. Grenet,[8] in his experi-

[3] Münch. med. Woch., 1902, p. 451.
[4] Trans. Assoc. Amer. Phys., 1911, xxvi, 178.
[5] Osler's Modern Medicine, vol. iv, p. 681.
[6] Semaine Méd., 1903, p. 153; 1904, p. 289.
[7] Amer. Jour. Med. Sci., 1909, p. 267.
[8] Comptes Rendu de la Soc. de Biol., 1903, p. 1509; ibid., p. 1568; Thèse, Paris, 1905.

mental studies on purpura, found that three factors were necessary for its production: (1) An hepatic lesion; (2) nervous injury, and (3) an intoxication which acted locally on the nervous system. He says that in purpura there is a toxin that acts as a vasodilator by means of the nervous system, and that if the blood is altered by a lesion of the liver or some other viscera then cutaneous hemorrhage results from the localized vasodilatation.

There have been two fairly constant changes found in the blood of purpura hæmorrhagica: The diminution in the number of blood platelets and the failure of the blood clot to contract and express the serum. Bensaude and Rivet[9] classify their cases of purpura according to the blood pictures into two groups. The first includes the simple, rheumatic, toxic, and nervous purpuras and is characterized by a contraction of the clot, with no diminution in the number of the blood platelets. The diminution of the blood platelets and the absence of the contractility of the clot are the characteristics of the second group, and in this group are placed all the forms of purpura with large subcutaneous hemorrhages and hemorrhages from the mucous membrane and viscera.

The occurrence of purpura, especially the hemorrhagic form, in the course of a tuberculosis is always a grave symptom. It either marks the terminal or cachectic stage of the disease or an acute exacerbation of the tuberculosis which may go on to a rapidly fatal termination or from which the patient may recover. But always after the attack of purpura the examination will reveal a more advanced condition of the lesion.

All my 8 cases occurred in the terminal stage of chronic pulmonary tuberculosis. Case I, was an undoubted case of purpura hæmorrhagica, and occurred only five days before death. Case II, although there was hematuria, and at one time bloody stools accompanying a diarrhea, was, I believe, a simple purpura; the hematuria being accounted for by the tuberculosis of the kidney, ureter, and bladder. Cases III, IV, V, and VI were undoubtedly instances of simple or cachectic purpura. The last 3 were not discovered during life. Case VII, where the thrombosis of the internal saphenous vein was the exciting cause, was what Osler calls a mechanical purpura, being caused by a venous stasis. My last case, Case VIII, might be called either a simple purpura complicating the tuberculosis or a toxic purpura complicating the intense jaundice. Whether, however, a simple or a toxic purpura it was a purpura occurring at the termination of chronic pulmonary tuberculosis complicated by a most unusual form of caseous tuberculosis of the liver.

CASE I, No. 2657.—An Italian boy, aged sixteen years, was admitted to the wards of the Phipps Institute, August 5, 1904.

[9] Loc. cit.

His father died at the age of thirty-three years of some unknown cause and his mother at the age of twenty-seven due to some accident incident to childbirth. He had an attack of influenza in February, 1904, otherwise had had no previous illness. He gave a history of having lost about 30 pounds in the last year and a half. He had had a hemorrhage from the lungs in December, 1903. Since April, 1904, he complained of cough, which was most troublesome at night, accompanied by a moderate amount of yellowish sputum. He had pain in the anterior aspect of his right chest, dyspnea on exertion, had had several attacks of hoarseness, poor appetite, vomited occasionally, and also had diarrhea. Formerly he had had night sweats and some edema of feet. The examination showed an emaciated boy, with no enlargement of the cervical, axillary, or inguinal glands, and no signs of curved nails or clubbed fingers. The heart showed nothing abnormal. The examination of the right lung showed a large cavity in the upper lobe, with more or less disease of the remainder of that lung. The left lung showed a possible cavity at the apex and some disseminated tubercles throughout the lung. There was in addition peritoneal tuberculosis. The boy was extremely ill, but had been doing well until September 15, about six weeks after his admission. At that time there occurred several small hemorrhages from the bowel, followed in a few hours by a marked hemorrhagic eruption over the abdomen. He complained of no pain. On the morning of the seventeenth his nose began to bleed and the hemorrhagic eruption appeared on the chest. In spite of plugging the nostrils the nose continued to bleed slowly, but persistently, all of the seventeenth and part of the eighteenth, and on the nineteenth there was still a tendency to bleed. The eruption on the nineteenth was most marked over the abdomen, it was fading in places but these were interspersed with fresher areas. Over the anterior chest there were scattered spots, as well as on both arms and on the back of the left wrist. On the back there were two or three small spots. There was no eruption over the pelvis or lower extremities. The patient died early in the day of September 20.

The autopsy performed later on that day showed an ulcerative and miliary tuberculosis of both lungs, pleural adhesions, parenchymatous nephritis, fatty liver, tuberculous enteritis, enterorrhagia, petechiæ in skin and in the pleura and pericardium, and enlarged mesenteric glands.

Case II, No. 2494.—A white man, aged twenty-three years, was admitted to the wards of the Phipps Institute June 10, 1904. His father had died at the age of fifty-five of heart disease. His mother, four brothers, and three sisters were living and well. Five brothers were dead, one having died of some disease of the bone and one of tetanus, the other three of unknown causes. One sister died in infancy. Three years before he had had an attack

of influenza and six months previously he had typhoid fever, followed in two months by rheumatism. In the last nine months he had lost twenty-two pounds, and complained of pain in both sides of chest in damp weather, cough, worse in the mornings, accompanied by considerable greenish sputum, marked dyspnea on exertion, occasional attacks of vomiting, diarrhea, night sweats, and slight edema of the feet. Examination showed an emaciated man. His heart was enlarged to the right and left. There was accentuation of both second sounds at the base. No murmurs were recorded. There was advanced disease of both lungs with cavities at both apices. His progress was fairly satisfactory for the first month, then he began complaining of painful urination with the passage of some gravel. His condition continued gradually to grow worse during August, his abdomen became distended and tympanitic, and he still complained of pain on urination, passing gravel and now also some blood. During September these symptoms continued, and on October 20, he developed a severe diarrhea, almost dysenteric in character, the stools containing much blood and mucus. By October 24, the diarrhea was greatly improved and there was no blood in the stools, but the patient was weak and losing ground rapidly. The diarrhea returned in a few days, but was not so severe as at first. On October 31, there appeared a purpuric rash all over the abdomen and extending up over the sternum to the level of the fourth rib. The patient died the next day.

The autopsy, performed the same day as the death, showed ulcerative and miliary tuberculosis of both lungs, pleurisy, tuberculosis of intestines, appendix, left kidney, ureter, and bladder, and cloudy swelling of right kidney, and enlarged mesenteric and bronchial glands.

Case III, No. 5473.—A woman, aged fifty-seven years, was admitted to the wards of the Phipps Institute, September 13, 1907. Her father had died at sixty-three of paralysis, and her mother at fifty-four of consumption. She had one brother living and well, three sisters living, two in good health, and one suffering with tuberculosis. Five brothers had died, one of consumption. She had had pleurisy and influenza two years before and rheumatism one year previously. She had not been well since her pleurisy, having lost over 60 pounds, and complaining of cough, worse at night, and in the early morning, accompanied by considerable yellowish expectoration. She had dyspnea on exertion, poor appetite, some slight soreness in epigastrium after eating, two loose stools a day, and slight edema of the ankles. A month previous to admission she had had night sweats. Menopause had taken place ten years before. Examination on admission showed an emaciated woman, with cheeks injected and slightly flushed, sordes on lips, and slightly curved nails. The heart was normal.

The examination of the lungs revealed an infiltration of the right upper lobe, a large cavity in the left upper lobe, a cavity in the upper part of the lower left lobe, with scattered infiltration below. The abdominal examination was negative. The course of the case was progressive, and in the beginning of October she developed a severe diarrhea. On October 10, about one month after admission, she showed on her forearms and legs a few small discrete, dark petechiæ, more marked toward the extremities. She died on October 21.

The autopsy showed chronic fibroid pleurisy of both sides, chronic empyema on the left side, chronic pulmonary tuberculosis of lungs with cavity formation, collapse of left lung from the empyema, emphysema (compensatory) of the right lung, interstitial myocarditis, atheroma of the aorta, cirrhosis of the liver with fatty infiltration, tubercles of liver, spleen and tonsils, ptosis of the intestines, chronic enteritis with tuberculous ulceration, chronic obliterative appendicitis, diffuse nephritis, and congestion of the spleen, tonsils, and mesenteric glands.

CASE IV, No. 2815.—A white woman, aged twenty-eight years, was admitted to the wards of the Phipps Institute on October 18, 1904. Her father died when aged forty years, of some unknown cause. Mother and one sister had died of phthisis. One brother and one sister were living and well. She had had pneumonia as a baby and malaria four years before admission. She gave a history of about 2 pounds loss in weight, cough with a small amount of greenish-yellow expectoration for nine months, some pain in shoulder blades, dyspnea on exertion, poor appetite, vomiting three weeks before, loose bowels, night sweats two months previously, slight edema of the feet, and the menses suppressed for four months. Examination showed an emaciated woman, with heart and abdomen normal, and advanced disease of the right lung, with cavities in the upper half and an infiltration of the apex of the left lung. The patient ran a rapid acute course and died on November 9, 1904.

The autopsy performed the next day showed ulcerative tuberculosis of both lungs with pleurisy, red atrophy of the liver, dilatation of the right heart, enlarged mesenteric and bronchial glands. There were noted on the inner aspect of the left thigh a few ecchymotic spots.

CASE V, No. 2664.—A white man, aged twenty-two years, was admitted to the wards of the Phipps Institute on August 8, 1904. His father, mother, two brothers, and two sisters were all living and well. He had had "typhoid-malaria" six years before and two attacks of pleuropneumonia, the first one two and a half years ago and the second one and a half years ago. Since his first attack of pleuropneumonia he had never been well, having lost about 45 pounds, and being troubled with a most distressing cough,

worse in the morning, and accompanied by considerable yellow expectoration. He had dyspnea on exertion, a fairly good appetite, three or four attacks a week of vomiting due to coughing, and regular bowel movements, recently a little streaked with blood. Examination on admission showed an anemic man not markedly emaciated. The abdomen was normal, and the heart showed mitral stenosis. The examination of the lungs revealed in the right upper lobe infiltration of the upper half, with miliary tubercles below, in the middle lobe miliary tubercles, in the lower lobe a close aggregation of miliary tubercles in the upper half and a few below, in the left upper lobe infiltration of the upper half and a close aggregation of miliary tubercles in rest of lobe, in lower left lobe a close aggregation of miliary tubercles in upper half and a few scattered below. The patient was in the hospital for six months, and was a sick man all the time, suffering greatly with dyspnea, distressing cough, and vomiting due to coughing. At the end of December and the first part of January he had several hemorrhages, one quite large, discharging over 10 ounces of blood. He continued spitting blood and suffering from his cough and dyspnea until he died on January 23.

The autopsy performed on January 24, showed a chronic tuberculosis of the lungs, with bronchopneumonia, chronic fibroid pleurisy of both sides, and parenchymatous nephritis. There were noted at autopsy a few red spots on the anterior surface of the abdomen.

CASE VI, No. 3451.—A white woman, aged twenty years, was admitted to the wards of the Phipps Institute on July 8, 1905. Her father died from drinking wood alcohol, and one brother died of hydrocephalus. Mother and two sisters are living and well. She had had influenza four years before. She gave a history that in the last eight months she had lost about 40 pounds, and had had for the last six months cough, worse at night, and accompanied by considerable yellowish-green expectoration, dyspnea on exertion, slight hoarseness at times, night sweats, variable appetite, vomiting at times, regular bowel movements, and suppressed menses for the last three months. Examination showed a fairly well-nourished woman. Her heart was normal, right kidney freely movable, otherwise the abdomen was normal. Lungs showed fairly advanced disease with a cavity in the right upper lobe. Her disease ran an acute course, and the patient died on November 13.

The autopsy performed the following day showed chronic fibroid pleurisy of the right side, chronic tuberculosis of the lungs, with cavity formation and edema, dilatation of the heart, atheroma of the aorta, fatty changes of the liver with congestion, and miliary tubercles, gastroptosis, tuberculous enteritis, diffuse nephritis, tuberculous adenitis, and tuberculous tonsillitis with amyloid

changes. It was noted that the face, back of the hands, chest, and shoulders showed a reddish-yellow discoloration. The inner surface of each leg had a few reddish-yellow blotches.

CASE VII, No. 2768.—A white man, aged thirty-three years, was admitted to the wards of the Phipps Institute October 3, 1904. His father died at the age of sixty-four years of typhoid fever. His mother, one brother, and five sisters were living and well. He had never been sick. He gave a history of cough and expectoration for two years. Three months before admission he had a hemorrhage from the lungs and his cough became more severe, with moderate amount of greenish expectoration. He suffered with dyspnea on exertion, slight hoarseness for a long time, frequent night sweats, and poor appetite, but no gastric symptoms. He had lost 50 pounds in the last three months. Examination on admission showed an emaciated man with a very hectic countenance. His heart was normal. Lungs showed advanced disease. There were cavities in the right upper and middle lobes and in the upper part of the lower lobe with miliary tubercles below. The left lung showed a small cavity at the apex with emphysema and miliary tubercles throughout the rest of the lung. Patient was extremely sick and very weak. He had an active miliary condition apparently following his hemorrhage three months previously. During the night previous to November 7 he was seized with a severe pain in the left leg. On the morning of November 7, the whole leg and thigh were slightly swollen with some pitting. There was cyanosis of the limb with numerous small purple spots which did not disappear on pressure. No special area of tenderness was found. In the afternoon of November 7, the pain was much less, and there was extreme tenderness on pressure on the veins in the popliteal area and for 3 inches upward. On November 9, his condition was much the same. He had had no return of pain and the tenderness was less. The purpuric spots were fading out a little. By November 14, the leg was no longer tender, but still retained some of the edema. He continued to grow weaker, and on November 23, died.

The autopsy performed the same day, showed a pneumothorax on the right side, effusion on the right side, caseous pneumonia of both lungs, with ulcerative tuberculosis of right lung, edema, and congestion of both lungs, fatty kidneys, displacement of liver, fatty infiltration of liver, pleurisy, enlarged bronchial glands, and thrombosis of the left internal saphenous vein.

CASE VIII, No. 2662.—A white woman, aged forty years, was admitted to the wards of the Phipps Institute August 8, 1904. Her father died at the age of forty-five years of tuberculosis. Mother died at the age of thirty years in confinement. She had one brother and one sister living and well. Two sisters died very young of some unknown cause. She had never been sick, but gave a history of excessive use of alcohol over a long period of time.

In the last two years she had lost 60 pounds, and for the last six months had had a cough, worse at night, accompanied by a profuse yellow expectoration. She complained of pain in lower anterior part of her right chest, dyspnea on exertion, attacks of hoarseness lasting several days at a time, poor appetite, epigastric pain, distress after eating, constipation, passing blood in the stools, night sweats, and slight edema of the ankles. Examination on admission showed an emaciated body, with a face of fairly good color. The heart was normal as well as the abdomen. The lungs showed infiltration of the upper part of the right upper lobe, consolidation with some softening of the left upper lobe. (This is a note made on the day of the examination that the prostration and loss of weight is out of all proportion to the pulmonary involvement.) On August 25, the liver was found slightly enlarged, edge very hard, but smooth and not tender. On September 21, the patient was markedly jaundiced; liver slightly enlarged. Pressure in the epigastrium caused a great deal of pain. No mass could be felt. On September 26, blood examination showed the erythrocytes, 3,840,000; leukocytes, 10,000. The blood was pale and coagulated slowly. The jaundice had become more marked. The conjunctivæ were of a bright yellow color. The whole body was now deeply jaundiced and pain in the epigastric region was more marked. Liver was distinctly palpable, and the edge was sharp and hard. The enlargement was more apparent in the left lobe. On October 1, the jaundice was intense, the abdomen flabby, and distended. There was some free fluid in the peritoneal cavity. Several purpuric spots appeared on the abdomen. From this time on the patient rapidly grew weaker, the jaundice being extreme, pain marked in the epigastrium, sordes on teeth and tongue, pulse weak and irregular, and she finally died on October 7.

The autopsy on October 8, showed ulcerated tuberculosis of the left lung, tuberculous pneumonia and edema of the right lung, miliary tuberculosis of the spleen, fatty infiltration of the heart, fatty kidneys, with tubercles, and an unusual caseous tuberculosis of the liver with cirrhosis.

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REVIEWS

A Treatise on Diseases of the Hair. By George Thomas Jackson, M.D., Professor of Dermatology in the College of Physicians and Surgeons, Medical Department of Columbia University, and Charles Wood McMurtry, M.D., Instructor in Dermatology in the College of Physicians and Surgeons, Medical Department of Columbia University, New York. Pp. 366; 109 engravings and 10 colored plates. Philadelphia and New York: Lea & Febiger, 1912.

In this treatise the authors have endeavored to present "all that is known about diseases of the hair and scalp;" and they have performed their task with a thoroughness and wealth of detail that has left no aspect of the subject unconsidered. It is divided into five sections: Anatomy, Physiology, and Hygiene of the Hair; Essential Diseases of the Hair; Inflammatory Diseases of the Hair Follicles; Parasitic Diseases of the Hair; and Diseases of the Hair Secondary to Diseases of the Skin.

The excellent chapter on the care of the hair and scalp concludes with a short section on barber shops and hair-dressing establishments which are regarded as "The most fertile single source of spreading diseases of the hair and scalp;" and some much needed advice is given concerning the proper management of such establishments, advice which if followed would go far to eliminate the danger of transmitting disease.

Among other important essential diseases of the hair the various forms of alopecia are considered at length. The authors regard some form of seborrhea as the exciting cause of one of the commonest forms of premature loss of hair, alopecia pityrodes; and they put themselves squarely on the side of the contagionists, declaring that "As seborrheal dermatitis and pityriasis steatoides are contagious diseases, and very prevalent, the wonder is not that so many people lose their hair, but that more do not." The parasitic origin of alopecia areata, however, which has many supporters, especially among the French, is not regarded as proved although it is not to be altogether rejected. Among the many medicinal agents recommended for stimulating the growth of hair in the several varieties of baldness pilocarpin is believed to be of decided value while crude petroleum which has long had a con-

siderable reputation, particularly among the laity, as a hair grower has been found useless.

The parasitic diseases of the scalp and beard are treated at great length, 65 pages being devoted to the subject of ringworm alone, a subject which is treated in a manner fully justifying the authors' statement made in the preface that "In no other book, excepting those of Sabouraud, will be found so complete a presentation of what is known about ringworm." Of the forty species of fungi concerned in the production of this very common malady enumerated by Sabouraud, twelve of the commonest are described together with the clinical symptoms and cultural features peculiar to each. In the treatment of this usually obstinate and troublesome affection preference is given to the *x*-ray when this is available, employing the technique of Sabouraud.

But one form of seborrhea is recognized, seborrhea oleosa, the seborrhea sicca of the text-books being in the opinion of the authors, not a seborrhea at all. This latter affection is described as pityriasis of which there are two forms, pityriasis simplex and pityriasis steatoides, the latter form being identical with eczema seborrhoicum. The bacterial origin of seborrhea is regarded as probable but not yet proved, but pityriasis simplex is believed to be caused by the organism first described by Malassez identical with the *flaschen-bacillus* of Unna.

The majority of the diseases discussed in the final section of the treatise, including such affections as, acne necrotica, psoriasis, lupus erythematosus, scleroderma, etc., are, of course, not diseases of the hair at all, but are included because they frequently occur upon the scalp or other hairy regions.

The volume is well illustrated, containing more than a hundred engravings and ten colored plates, most of them of unusual excellence, which add much to its value.

In conclusion, this treatise which is remarkably complete and up to date, is easily the best work upon diseases of the hair which has yet appeared. M. B. H.

PHARMACOLOGY AND THERAPEUTICS. By H. C. WOOD, JR., M.D., Professor of Pharmacology and Therapeutics in the Medico-Chirurgical College of Philadelphia. Pp. 429; 26 illustrations. Philadelphia: J. B. Lippincott Co., 1912.

IN his text-book on Pharmacology and Therapeutics, Dr. Wood writes clearly and concisely and with not more than the necessary dogmatism. He has eliminated non-essentials and confusing discussions of facts which are of doubtful interpretation. His grouping of drugs is based on what he considers their most important therapeutic application, and as therapeutics is emphasized as strongly as pharmacology, such an arrangement is a logical one.

At the conclusion of the account of each drug, a short bibliography is inserted covering the more important publications concerning them. Some slight criticism may be offered of this feature of the book. The list of references is, at times, too curtailed. For example, under digitalis, none of the numerous and important contributions of Hatcher is mentioned. Again it would seem desirable to indicate what particular reference has to do with certain facts given in the text, since otherwise it might become necessary to look through the entire list before the original authority for a statement is found.

With regard to other features of the book, it is unfortunate that at a time when teachers of prescription writing are urging the use of the metric system, and when this system is given preference in the pharmacopœia, Dr. Wood should place more emphasis on the system of apothecaries' weights and measures. In his chapter on prescription writing, he uses the latter entirely in his prescription examples, and again in the dosage given for each drug, this system is given first place.

Concerning the matter in the text in general, the chief criticism is that too much brevity has been exercised. For example, no mention is made of antitoxins and vaccines, which have now a very definite place in therapeutics. In the chapter on bromides, no mention is made of the inter-relationship of bromides and chlorides, a matter of considerable pharmacological interest and therapeutic importance. In the introductory chapter on the mode of administration of drugs, the technical aspects of the subject should be described at greater length. It would be quite proper, for example, to give a full description of the method of intravenous injection. This would be directly applicable to the administration of salvarsan in syphilis, and an authoritative statement of the technique of neutralization and injection of this drug would be of value to readers of the book. The author's apparent preference for giving mercury by the stomach in the treatment of syphilis will undoubtedly not be approved by the majority of syphilographers, who believe so thoroughly in intramuscular injection.

Under the digitalis group, the therapeutic uses are prescribed in far too condensed a form. This subject has been studied extensively by Cushny and others, and the conclusions arrived at are of the greatest importance to the practitioner. Cushny has also called attention to the infrequent occurrence of the so-called cumulative action of digitalis, and has emphasized the fact that vomiting is the first and usually the only symptom of overdosage during continued medication. The work recently done along these lines should by all means be incorporated in the text.

On the whole, Dr. Wood's book shows great industry and familiarity with recent literature, and omissions such as have been noted are perhaps to be expected in a first edition. G. B. W.

SURGICAL AFTER-TREATMENT. By L. R. G. CRANDON, M.D., Assistant in Surgery at Harvard Medical School, and ALBERT EHRENFRIED, M.D., Assistant in Anatomy at Harvard Medical School. Second edition. Pp. 831; 264 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

THE success which this work has had causing a revision and second edition in so short a space of time, is commentary enough upon its need and value.

As its name implies, this is simply an after-treatment to surgical procedures and as such should prove of the greatest value not to surgeons alone, but to those also who not being surgeons are left in charge of cases when the services of the surgeon are no longer available. This is especially true if the case has been left under the care of a practitioner who has not had any recent surgical experience.

The authors have divided the book into two parts. In the first there are thirty-nine chapters devoted to the care of the patient and the alleviation of various symptoms. Here many practical points are brought up which the young house surgeon is only too apt to leave to the nurse and which the busy practitioner out of touch with modern hospital methods is often at a loss to know how to handle.

The subject of the treatment of the patient after the administration of an anesthetic and the various methods for relieving the nausea and vomiting and the accompanying thirst are carefully taken up. The manner of giving enteroclysis is correctly shown, and similar treatments are likewise elucidated, all of which are rational and good. In addition, the illustrations which accompany the descriptions are excellent and are of the greatest practical assistance in making the text clear.

Not only to the physician will these chapters in the first part of the book be of use, but to the nurse as well, especially should she happen to be one who has had only a limited training in the care of the sick.

The discussion of bandaging, though brief, is to the point, and covers most of the important facts upon that subject which are essential in such a work.

There are certain chapters in this section such as Foreign Bodies Left in the Abdominal Cavity, Adhesions, and Preparation of the Patient for Operation, which hardly come within the scope of a book upon surgical after-treatment, and which could well be omitted and the book improved by thus having its bulk diminished.

In the second part the remaining fourteen chapters of the book with the exception of the last two, are devoted to various operations and their after-treatment. In these chapters the authors are clear and concise and do not confuse the reader by too many

methods, usually limiting themselves to one good method of treatment. Here, too, the illustrations are numerous and well chosen and greatly add to the text.

Very carefully and completely are the various parts of the body, with the operations peculiar to each, taken up and systematically discussed.

The last chapter but one is devoted to Therapeutic Immunization and Vaccine Therapy and has been most ably presented by Dr. George P. Sanborn, but is somewhat out of place in a work designed primarily for the practitioner rather than the specialist.

Throughout the whole work the authors have maintained an unusually high standard, and such a book cannot help but be of the greatest assistance to anyone who wishes to keep up with modern methods of surgical after-treatment.

F. P., JR.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., at Mercy Hospital, Chicago. Volume I, No. 4. Pp. 154; 22 illustrations. Philadelphia and London: W. B. Saunders Company, August, 1912.

AMONG the most important of the many subjects discussed in the August number of Murphy's clinics are ankylosis of the knee, arthroplasty, and joint infection; hypertrophy of the prostate; old fracture of the elbow-joint; traumatic epilepsy, with decompression; carcinoma of the lip; and finally, a Student's Clinic, at the Northwestern University Medical School, devoted to a quiz on the subject of fractures, and to a discussion of joint infections.

There is no denying the interest which attaches to this series of publications. Though second thought and careful revision would, no doubt, make even Dr. Murphy desire to modify some of his statements and expunge others, it is not likely that any one of experience will take this magazine for other than it is—a stenographic report of clinics. It has neither the accuracy nor the system of a monograph, and if one wanted either to learn cold facts of science or to study details of operative procedure he certainly would not look in a publication which professedly comes red-hot from the printing press, and which even to casual inspection reveals such lack of editing as in a daily newspaper might be condoned, but which could not be overlooked in a monthly or quarterly periodical claiming for itself a certain literary prestige. Yet there are monographs and text-books in abundance, but only one "Murphy's Clinics;" and with all its faults we love it still. A. P. C. A.

THE PRACTICE OF MEDICINE. A MANUAL FOR STUDENTS AND PRACTITIONERS. By HUGHES DAYTON, M.D., formerly of the Cornell University Medical School, New York. Second edition. Pp. 326. Philadelphia and New York: Lea & Febiger, 1912.

DAYTON, in this epitome of internal medicine, presents to the hurried practitioner and the undergraduate student, a brief treatise on the essentials of diagnosis and treatment. The classification of the various diseases, as well as the general form of presenting them, follows closely that used in Osler's practice. The salient features of the etiology, pathology, symptomatology, differential diagnosis, prognosis, and treatment of most diseases are described in a concise, brief, but thorough manner. The less important diseases are also carefully elucidated, but on account of the character of the book, the same attention cannot be directed to them as to the more frequent and hence, more important diseases.

The criticism of this book is such as applies to all books of this character. Disease presents so many variations and aspects that a brief description of a typical case can at the best be only suggestive. Hence, to elaborate the suggestions that have been conveyed to the reader recourse must be had eventually to the larger and more complete text-books.

There is no criticism to be made of the subject matter, which briefly includes the more recent advances in medicine, nor of the general appearance of the book, which is neat, well printed, and free from typographical errors. J. H. M., JR.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor of Therapeutics in the Jefferson Medical College, Philadelphia. Vol. III, September, 1912, pp. 353; 28 illustrations. Philadelphia and New York: Lea & Febiger.

As each successive number of *Progressive Medicine* comes to our attention we become increasingly impressed with the unquestioned merit and excellence of the contributions and the value of this publication to every practitioner who would keep abreast of the time.

Volume III for this year opens with a article of 86 pages by William Ewart on diseases of the thorax and its viscera. He begins by taking up tuberculosis and its treatment; he next dis-

cusses recent advances in percussion and auscultation of the chest; this is followed by a consideration of pulmonary edema, emphysema, pulmonary surgery, mountain sickness, compressed air illness, common colds, asthma, and an exhaustive review of the subject of atmotherapeutics. Under the heart and great vessels he discusses the various newer instruments of precision, certain physical signs that have recently attained importance, some interesting cardiac affections including paroxysmal tachycardia and "cardiac asthma," and heart treatment. He concludes with several pages devoted to a number of affections of other mediastinal organs.

William S. Gottheil calls attention to recent advances in dermatology and syphilis in a contribution of 40 pages. Among many interesting subjects considered are: Blue atrophy of the skin from cocaine injections, the early diagnosis of cancer of the skin, chancroid vaccine, the rational treatment of furunculosis, pruritus ani, and lichen planus in the negro. The last quarter of his article deals entirely with syphilis.

The contribution on obstetrics is furnished by Edward P. Davis, who devotes 150 pages to this important subject. He first takes up the diagnosis of pregnancy; then the urine in pregnancy; various phases of the toxemia of pregnancy; gestation complicated by tuberculosis and various other conditions; as well as many other important phases of the subject, notably eclampsia and placenta prævia. Under labor he discusses among other things labor during adolescence; complications of labor; and the treatment of labor complicated by operation for antefixation. The uterine muscle, abortion, and pituitrin are also considered and his excellent *resume* of the subject concludes with interesting sections on obstetric surgery, the puerperal period, and affections of the newborn.

The final chapter of the volume is by William G. Spiller, from whom we have learned to expect without fear of disappointment an able discussion of diseases of the nervous system. His present review of the subject embraces 52 pages and is fully up to the high standard he has set in all his previous contributions. G. M. P.

THE PITUITARY BODY AND ITS DISORDERS. CLINICAL STATES PRODUCED BY DISORDERS OF THE HYPOPHYSIS CEREBRI. By HARVEY CUSHING, M.D., Associate Professor of Surgery in the Johns Hopkins University, Professor of Surgery (elect) Harvard University. An amplification of the Harvey Lecture for December, 1910. Pp. 341, with 319 illustrations. Philadelphia: J. B. Lippincott Company, 1912.

DR. CUSHING with his usual originality has succeeded in arousing the attention of the medical profession. He has collected an

enormous amount of material regarding the pituitary body much of which is original and the result of careful clinical observation and experiment. Not all the statements that he makes in all probability will be confirmed by further study, but of this fact he is keenly aware. His book is that most valuable of all forms of medical publications, a painstaking monograph, and should appeal to many classes of the medical profession, to the physiologist, to the surgeon, and above all to the clinician.

The four main types of pituitary disease are gigantism and acromegaly produced respectively it is supposed by overaction of the pituitary gland in youth and in adult life; infantism and adiposity produced by the deficient action of the gland before and after puberty. Combinations occur and we are not yet able to differentiate with precision all the functions of the different parts of the gland, but at least the material available for our knowledge has been presented in a clear and logical manner.

The number of illustrations is remarkable, but they are all illustrative and there is actually no padding, a fault that few medical books escape. Perhaps the most useful original communication is the attempt to devise a method of administering pituitary extract in a rational and adequate manner to cases needing it. A few typographical errors have crept in, but they do not apparently in any instance mar the clearness of the text. The taste of the reviewer is against the splitting of the infinitive but Dr. Cushing appears to prefer it. It has at least the authority of frequent usage at the present day.

The work is a distinct contribution to medical literature, perhaps one of the most notable of the year. J. S.

DISEASES OF THE STOMACH WITH ESPECIAL REFERENCE TO TREATMENT. By CHARLES D. AARON, Sc.D., M.D., Professor of Gastro-enterology and Adjunct Professor of Dietetics in the Detroit College of Medicine; Professor of Diseases of the Stomach and Intestines in the Detroit Post-graduate School of Medicine, Consulting Gastro-enterologist to Harper Hospital. Pp. 555, with 42 illustrations and 21 plates. Philadelphia and New York: Lea & Febiger.

DR. AARON has contrived to write a work upon diseases of the stomach and to avoid more or less completely the conventional lines of the text-book. The material that he has included is somewhat unusual and it almost seems as if he had kept a notebook in which he recorded various things that might be useful in his practice and had later incorporated the best of these in his book.

It is obvious that it is not possible in a work of this kind to be wholly original, but Dr. Aaron manages frequently to present old facts in a refreshing manner.

The first part of the book is devoted to physiology and methods. A somewhat ambitious effort is made to reproduce the color reactions, but as these can be learned so readily in the laboratory with artificial solutions and as the reproductions of the colors are never absolutely exact, the result is not always satisfactory. In the chapter on diet tables are introduced of the various types of diet, the European origin of which has not been as completely disguised as one would like in an American text-book. Then follows several chapters on methods of treatment, that on hydrotherapy being particularly useful, and a very valuable chapter upon surgical intervention.

Dr. Aaron has not successfully resisted the temptation to devise an abdominal bandage and corset, but if this is a fault it is so commonly perpetrated by those engaged in the study of diseases of the gastro-intestinal tract that he should receive ready absolution. The functional diseases of the stomach, particularly motor insufficiency are well discussed and there is a valuable chapter upon gastric hemorrhage.

Altogether the book can be commended as one of the best of the recent works published on the subject. J. S.

PRIMARY MALIGNANT GROWTHS OF THE LUNGS AND BRONCHI. By I. ADLER, A.M., M.D., Professor Emeritus at the New York Polyclinic. Pp. 325; 16 plates and a colored frontispiece. New York, London, Bombay, and Calcutta: Longmans, Green & Co., 1912.

THIS very scholarly monograph, which represents a vast amount of labor in its compilation, will fill an important place among reference handbooks concerning a condition little known and seldom considered in the differential diagnosis of diseases of the chest. It will serve also to focus more attention on the possibility of malignancy in doubtful cases. The author desires to bring home the fact that primary tumors of the lungs are not so exceedingly rare as is commonly supposed, and remarks justly enough that for the majority, "the ubiquitous tuberculosis with its multiform clinical appearances, and its plastic adaptations to all ages and all conditions of mankind, is ever ready to furnish to all but a very few, a comfortable and satisfactory diagnosis."

Of the 325 pages, 105 are devoted to a consideration of the etiological, pathological, and clinical features of pulmonary neo-

plasms (excluding primary growths of the pleura). The remaining 220 pages are taken up with analytical tables of all cases reported up to the time of publication, comprising 374 cases of carcinoma, 90 cases of sarcoma, 99 classified as doubtful, and 18 miscellaneous tumors. Tables are appended with figures concerning the duration of life in carcinoma and sarcoma cases and the location of metastases.

Adler states as the present consensus of opinion that primary carcinomas of the lung develop from the bronchi and are strictly bronchial carcinomas; that on the other hand, carcinoma starting from lung tissue does occur, but is very rare and is built up not of flat but of cylindrical epithelium. He discusses at some length the nature of endotheliomas, and shares the views of those who oppose the classification of tumors according to the three germinal layers. Another chapter deals in an interesting manner with the various conflicting views concerning metaplasia, not, however, with reference to pulmonary neoplasms in particular.

In the description of the clinical features associated with malignant growths in the lungs, the following symptoms appear most prominently. In the early stages, a rather insignificant but fairly constant cough, mostly without expectoration; the presence in the sputum of large spherical cells filled with a multitude of fatty granules; paralysis of the recurrent laryngeal nerve in the presence of malignant effusions; and a loss of weight and strength. As aids to diagnosis, he urges the routine use of the *x*-rays, and of the bronchoscope, which, he believes, is of use in detecting the growths occupying the upper bronchi. He urges in suspected cases, the practice of exploratory thoracotomy. The plates, chiefly representing histological preparations, are for the most part admirable. H. G. S.

THE PRINCIPLES OF ANATOMY. THE ABDOMEN PROPER DESCRIBED AND ILLUSTRATED BY TEXT AND PLATES. By WM. CUTHBERT MORTON, M.A., M.D. (Edin.). Pp. 159; 28 illustrations. New York: Rebman Company.

ONLY the abdomen is considered in this the first portion of what is intended to be a work on the anatomy of the whole body. Morton presents a method of studying anatomy which differs considerably from that usually employed in medical schools. It is intended not to rival, but to stimulate practical study, and to unify the host of impressions gained at the dissecting table, in the lecture room, at the bedside, and in the operating room. It substitutes for the usual text-book, made up chiefly of text with more or less profuse illustrations; a small text-book in which there are a few illustrations, and a series of 28 large plates or 14 front-and-

back plates. The book, after discussing the underlying principles of the method and the plates, which are kept separately in a portfolio, gives directions for the dissection of the abdomen. Then follows the descriptive text, which is largely a brief outline of the various organs and other structures, and is apparently supplementary to the plates. These are artistic, but purely diagrammatic, and presumably as accurate as such illustrations can be. Each plate may be inspected separately, or by transillumination, when the whole of each organ can be seen in outline and the front and back plates correlated with each other. By combined inspection by means of cut-out leaves, one obtains a front view of certain organs lying at different depths and a similar back view of others.

A trying out of the method will be necessary to determine its value. The finding and tracing of the various structures on the plates, after the reading of the text, will tend to fix the facts more firmly in the student's mind, but it is possible that this will be at the expense of too much time, because of the necessary frequent passing from text to illustration, which is not aided by signs or numbers. Nor is it evident that the impression left in the student's mind is clearer and more lasting than that obtained by the usual method of study. The same time given to the accepted text-books, the various models, and cadaver preparations, dissections and sections, usually available to the present-day student, would probably give better results. A book on anatomy must be incomplete which does not include a consideration of microscopic anatomy, but this could hardly be expected in a work the chief object of which is to teach by illustrations. T. T. T.

My Method of Preparing the Operative Field With Tincture of Iodine. By Kgl. Rat Dr. Antonio Grossich, Chief Surgeon of the City Hospital in Fiume. Pp. 80. Berlin and Vienna: Urban & Schwarzenberg.

Grossich presents, in the form of a monograph, his conception of the position now occupied by his iodine method of preparing the skin of the operative field. That it has been a valuable contribution to operative surgery needs no discussion. In the four years since its introduction its recognition has become world-wide, and this full presentation of the whole subject will receive, undoubtedly, a cordial and wide reception. It is a general summing up of the work done by Grossich and others. He discusses his experience in 3759 surgical and gynecological cases, dividing them into those of accidental wounds, aseptic and septic operations, and emphasizes especially its value in the treatment of accidental

wounds. A separate section is devoted to the various objections raised against the method, such as the development of eczema, adhesions between coils of intestines from irritation due to contact with the iodine-covered abdominal skin during the operation, and conjunctivitis. The importance of avoiding all washing before applying the iodine is emphasized. Those who wish to become familiar with the method in all its details will find here all the necessary information, including a brief abstract of all papers published on the subject. T. T. T.

AN INDEX OF TREATMENT BY VARIOUS WRITERS. Edited by ROBERT HUTCHISON, M.D., F.R.C.P., Physician to the London Hospital, etc., and H. STANSFIELD COLLIER, F.R.C.S., Surgeon to St. Mary's Hospital, Joint Lecturer on Surgery in St. Mary's Hospital Medical School, etc. Revised to conform with American usage. By WARREN COLEMAN, M.D., Professor of Clinical Medicine and Applied Pharmacology, Cornell University Medical School, etc. Sixth edition, revised and enlarged. Pp. 1051; 67 illustrations. New York: William Wood & Co., 1912.

THE demand for short-cut methods in the practice of medicine is much in evidence at the present time, as shown by the numerous digests of literature, compends, and in the present instance in the demand for a sixth edition of the work before us. The effect of these short-cut methods on general medical work may be questioned. There is already too much of a tendency among physicians to superficiality and symptomatic treatment without striking at the root or actual cause of the disorder, and we fear that these condensed and abbreviated compends rather foster than discourage this tendency.

In the present work the authors have attempted to provide the practitioner with a complete guide to treatment in moderate compass and in a form convenient for reference. They have been fortunate in securing the coöperation of a group of contributors of special experience whose names will be a sufficient guarantee of the value of the text, and no pains have been spared to make the book a trustworthy index to the best and most modern methods of dealing with disease. In the present edition all of the old articles have been thoroughly revised and many new ones included, among which are those on puerperal sepsis, hydro- photo- and thermotherapy, and treatment by carbonic snow, along with a good number of shorter ones.

The work is remarkably thorough for a work of its kind, and covers a multitude of subjects. The individual articles have the

signature of the contributor, adding considerably to their trustworthiness. The directions are clear and concise, and confine themselves usually to one line of treatment which has been tried and proved to be reliable. With a work of such broad scope there are bound to be minor omissions, and the present volume is not free from this error. The treatment in some instances falls into the fault of being too symptomatic and shotgun in type. The drugs and prescriptions, although made to conform in the main to American usage, nevertheless bear their English stamp. The printing while small is unusually clear and distinct, the paragraphs well-marked, and the entire work remarkably free of typographical errors. While we would hesitate to recommend the book as a single book to be depended on, it is certainly an addition to our books of handy reference so useful in the hustle of busy practice. It should, however, be used along with works on general diagnosis and pathology. F. H. K.

THE SKIAGRAPHY OF THE ACCESSORY NASAL SINUSES. By A. LOGAN TURNER, M.D., F.R.C.S.E., F.R.S.E., Surgeon to the Ear and Throat Department, the Royal Infirmary, Edinburgh; Lecturer on Diseases of the Ear, Nose, and Throat, University of Edinburgh, and W. G. PORTER, M.B., B.Sc., F.R.C.S.E., Surgeon to the Eye, Ear, and Throat Infirmary, Edinburgh. Pp. 127, with 45 half-tone reproductions from radiographs and 3 drawings. Edinburgh and London: William Green & Sons, 1912.

THIS book seems to represent an effort on the part of the authors to demonstrate to their fellow specialists the assistance to be gained by radiography in the diagnosis of accessory sinus disease, and to aid in the difficult interpretation of the complicated radiographs of the head. With these ends in view, the authors have succeeded admirably in their purpose. The handling of the subject by rhinologists renders it better adapted, perhaps, to the comprehension of the followers of this specialty than would be the case if it were presented from the standpoint of the Röntgenologist. The former is made to realize just what dependence he can place upon radiography to aid him in diagnosis. The Röntgenologist who has had but a limited experience in sinus work will find much of value in this book to aid him in learning to identify anatomical landmarks in his plates and to properly interpret the evidences of disease. The authors have included a study of sinus development in infancy and childhood from the *x*-ray standpoint, and have demonstrated the wide variations from any fixed standards that may be readily shown at different ages. H. K. P.

DIAGNOSE UND FEHLDIAGNOSE VON GEHIRNERKRANKUNGEN AUS DER PAPILLA NERVI OPTICI. By PROFESSOR DR. FR. SALZER, of Munich. Pp. 16; 29 illustrations in 2 colored plates. Munich: J. F. Lehmann.

THE author observes very justly that the ophthalmoscopist, perhaps even to a greater degree than he is himself conscious, is wont to control the objective appearances in the fundus, particularly choked disk and atrophy, by the history and subjective examination, both of which frequently fall away in psychic disorders, which latter are so often brought under his notice. The very fact that all the details are recognizable with such exactness with the ophthalmoscope adds to the difficulties of the situation. Uncertainty in objective diagnosis is due principally to two important circumstances: (1) The extraordinary degree of variability in the ophthalmoscopic picture of the normal papilla and its immediate surroundings, and (2) that the modifications of the picture occasioned by important pathological processes are frequently so slight.

Of the two excellent colored plates, the first containing 20 pictures taken from life, exhibits the great variability of the normal papilla. Eight pictures of the second plate are examples of pathological or doubtful findings. The variations indicated in both concern the color, outline, and relief of the papilla and the bloodvessels. The author insists that a diagnosis of either pallor or heightened color should only be made upon the basis of two or more examinations made at different times. A detailed description of each picture is given in the text. As a final justification the writer cites the lack of concordance in the statistics as to the percentage of pathological findings given by different observers in the same diseases. (Some of these divergences depend, of course, upon differences in the material.) T. B. S.

THE BACILLUS OF LONG LIFE. A MANUAL OF THE PREPARATION AND SOURING OF MILK FOR DIETARY PURPOSES, TOGETHER WITH AN HISTORICAL ACCOUNT OF THE USE OF FERMENTED MILKS, FROM THE EARLIEST TIMES TO THE PRESENT DAY, AND THEIR WONDERFUL EFFECT IN THE PROLONGING OF HUMAN EXISTENCE. By LOUDON M. DOUGLAS, F.R.S.E. Pp. 163; 62 illustrations. New York and London: G. P. Putnam's Sons.

THIS volume is the twenty-ninth of the "Science Series" published by this firm. In each volume of this series a single author attempts to present his subject in a form at once accurate, scientific, and intelligible to the general reader. Certain volumes published in this series are well known and deserving of great praise, as, for example: *Fatigue*, by Mosso and others. The subject of the

present volume does not lend itself readily to this style of exposition, and the result has not been happy.

The first two chapters of the book are much the best, the first a short historical introductory account of the use of milk as a food, and the second, a description of the various fermented or soured milks used throughout the world. Both these chapters are filled with quotations, with references from works of travel and history which render them interesting.

The remaining chapters on the chemistry and handling of milk, the bacteriology of fermented milk, its preparation in the house and in the dairy, and finally, a consideration of the use of soured milk in health and disease, are of much less interest; especially is the section on the chemistry of the milk most unsatisfactory. It is unnecessary here to repeat the extravagant claims which have been made for soured milk, all of which the author faithfully includes.

On the whole, the book does not fulfil any purpose, and cannot be recommended. O. H. P. P.

MODERN MICROSCOPY. A HANDBOOK FOR BEGINNERS AND STUDENTS. By M. I. CROSS and MARTIN J. COLE, Lecturer in Histology at Cooke's School of Anatomy. Fourth edition. Pp. 325; 113 illustrations. Chicago: Chicago Medical Book Co., 1912.

THIS is a book primarily for the man with a general interest in what the microscope will show of the world about him. At the present time, it must be acknowledged that this class is not a large one, and the societies which devote themselves to purely microscopical science are likewise much reduced in number. In the modern specialization of all science, the microscope has been treated more and more as a tool, and interest in it as an instrument has become subordinate to the various scientific branches in which it is used. It is the laudable effort of the authors to keep alive something of the old spirit and to direct interest outside of the narrow sphere of every-day work.

Part I comprises five chapters devoted to the microscope and its accessories. Part II consists of fifteen chapters, giving methods of examination of animal and vegetable tissues, including mounting of microörganisms, crystals, diatoms, etc. Part III, new in this edition, comprises special chapters by various writers, on the petrological microscope, rotifera, freshwater mites, mosses and liverworts, microscopy of foods, and other subjects.

This book cannot fail to be interesting to the beginner who wishes to master the principles and exact manipulation of the microscope or to anyone with the inclination and lesiure for a general study of Nature. W. H. F. A.

UROLOGISCHER JAHRESBERICHT. Edited by DR. A. KOLLMANN and DR. S. JACOBY. On Literature of 1910. Pp. 460. Leipzig: Werner Klinkhardt.

THE editors, with the assistance of a large number of colaborators, have prepared a valuable volume, which permits a rapid review of the important papers, published in 1910, on affections of the urinary tract and on affections of the male genital system. The abstracts are grouped together into those on anatomy, physiology, pathology, and the chemistry of the urine. The great majority fall into the group under pathology, where they are further classified into those affecting the kidneys, ureters, bladder, etc. Some conception of the material represented in this review can be obtained from the fact that more than 1300 papers are abstracted, 319 under pathology, on the surgical affections of the kidneys and ureters. The volume is calculated to give, probably, as brief and at the same time as comprehensive a review of the literature of genito-urinary surgery for 1910 as could well be prepared.

T. T. T.

MANUAL OF PHYSIOLOGY. By H. WILLOUGHBY LYLE, M.D., B.S. (Lond.), F.R.C.S. (Eng.). Pp. 747; 137 illustrations. London: Oxford University Press.

THIS book covers, in a sufficiently comprehensive manner that which is required of a manual of physiology. The material is well selected and concisely and clearly described. Naturally, much which is found in the larger text-books, must be omitted in a work of this kind. However, by economizing space by omitting histology, except that absolutely necessary for purposes of description as well as embryology, and limiting the reference to experiments to a minimum, a proportionately large amount of purely physiological data is introduced in its 747 pages. Physiological chemistry receives a fair amount of attention, and some of the most used tests are described. The author has given such subjects as are of immediate value to medicine and surgery considerable space. For example, a chapter is devoted to inflammation, although, it is true, it is a short one. Elsewhere, too, we see frequent references to subjects of practical value to the clinician. But the book does not serve in any way as a guide to a laboratory course in practical physiology, nor does it intend to. This omission is wise, as much space is economized and then, again, books covering this field exclusively are now necessary for every medical student. As a manual, however, the book serves its purpose admirably.

E. L.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Results of Antityphoid Vaccination in the Army in 1911, and its Suitability for Use in Civil Communities.—FREDERICK F. RUSSELL (*Jour. Amer. Med. Assoc.*, 1912, lviii, 1331) reports that antityphoid vaccination in the army has been carried out as follows: An avirulent culture of the typhoid bacillus is grown for twenty-four hours on agar, washed off in normal salt solution, standardized by counting the bacilli, killed by heating to 55° C. for an hour. Twenty-five per cent. tricresol is added as a matter of safety. This vaccine is injected subcutaneously in three doses at ten-day intervals. The first contains 5 million bacteria, the latter two a billion. As a rule, there is a local reaction consisting of a red and tender area about the size of the palm of the hand, subsiding within forty-eight hours. A severe general reaction occurs in only 1 to 3 persons per thousand. Since 1908, approximately 100,000 vaccinations have been made with no accidents. The effect on the morbidity from typhoid is now becoming apparent. From its use under conditions in the army, Russell believes that anti-typhoid vaccination in healthy persons is harmless and efficient, since it confers almost absolute immunity against infection under all conditions, assuredly for two and a half years, and probably longer. Thus the general vaccination of an entire community is feasible, and should be urged wherever the typhoid rate is high.

Secondary Infections in Ulcerative Tuberculosis of the Lung.—A. VEILLON and G. REPACI (*Annales de l'Institut Pasteur*, Paris, 1912, xxvi, 300) have studied the question of secondary infection in tuberculosis in the following manner: Smear preparations, animal

inoculations, and cultures on aërobic and anaërobic media were made from tuberculous sputum, cavities or lung tissue at autopsy, and from the circulating blood. By this method the cases studied fell into three groups. (1) A small number of cases in which no other organisms save tubercle bacilli were found. (2) A large number of cases in which the common aërobic organisms were found, never, however, in lung tissue or blood. Thus Veillon and Repaci think that such bacteria may remain in tuberculous cavities for a long time without causing complications. (3) A large number of cases in which anaërobic organisms were grown from sputa, cavities, and lung tissue. They consider this group of especial importance. In such cases clinically, the sputum is often colored and foul, giving to the breath a characteristic odor. Pathologically, in addition to tuberculosis, the lung shows evidence of putrefaction. Since these organisms penetrate deeply into the tissue, small areas of gangrene may appear, and by rupturing into the pleural cavity may cause a putrid pleurisy. On the whole, Veillon and Repaci believe that anaërobic infection gives to tuberculosis special features, characterized by foul sputum and gangrene of the lung with resultant aggravation of the patient's general condition.

Aortic Aneurysm of Rheumatic Origin.—P. Emile Weil and P. J. Ménard (*Bull. et Mém. Soc. méd. d. hôp. de Paris*, 1912, 3d, 491) describe a case of aneurysm of the ascending arch of the aorta, with aotic insufficiency, in a woman, aged forty-four years. There was no evidence of hereditary or acquired syphilis. The Wassermann reaction was negative. The family history was rheumatic, and when four years old the patient had suffered a severe attack of polyarticular rheumatism with subsequent less severe attacks every winter. From the facts that aneurysm, with typical clinical and radioscopic signs seemed to follow the rheumatism, and with history negative in other respects, it seems logical to consider the lesion of rheumatic origin. Doubtlessly, syphilis must be considered the most frequent cause of aneurysm. It is not the only one. From a careful review of the literature Weil and Ménard believe it is established both from pathological and histological standpoints: That aneurysms may develop after general infections, and rhematism particularly. Clinically Weil and Ménard conclude that aneurysms of this etiology have essentially the following features: They develop in young people usually aged under thirty years, following one or more attacks of acute rheumatism. The most frequent location is on the ascending portion of the aortic arch accompanying a valvular lesion, usually aortic insufficiency. The outcome is rapid. [One wonders whether some of these instances of "rheumatic" aneurysms may not represent that remarkable dynamic pulsation of the elastic aorta sometimes met with in aortic insufficiency in the young.—W. S. T.]

Mechanical Production of Fever.—A. Bock (*Archiv f. exp. Path. u. Pharmakol.*, 1912. lxviii, 1) has investigated the possibility of producing fever simply by mechanical irritation. All observations have been made on experimental animals. He arrives at the following conclusions: (1) The sodium ion has the specific property of raising body temperature. Intravenous injection of 20 c.c. of sterile Ringer's

solution has no effect on the temperature, while physiological salt solution practically always causes an elevation. (2) Injection of 20 c.c. paraffin suspension with a content of 0.01 to 0.1 per cent. of paraffin and 2000 to 11,000 particles of paraffin per 1 c.mm. regularly leads to elevation of temperature of ½ to 1° C. and more. (3) Injections of electrargol and electroplatinol produce fever. (4) Injection of Ringer's solution with 0.1 to 0.3 mg. arsenic per kilo of weight (rabbit) is followed by a rise in temperature. Fifty times this dose causes an immediate fall. (5). The fever following the injection of fine suspensions of paraffin, silver, and platinum may be due to a mechanical irritation of the sympathetic nerve endings in the vessel walls or to the action of products of metabolism of the leukocytes, which are formed as a response to the introduction of the foreign material.

Experimental Digestive Leukocytosis.—M. BRASCH (*Zeitschr. f. exp. Path. u. Therap.*, 1912, x, 381) approaches the question of digestive leukocytosis, about which there has never been unanimity, from the experimental side. He records numerous experiments on rabbits and dogs and finds that a digestive leukocytosis follows the taking of food during hunger practically without exception. The kind of food seems to be of minor importance, as it was observed to occur after giving nucleic acid, protein, fat, and carbohydrate. The leukocytosis appears within four to ten hours after the food is given. In rabbits it is generally the small lymphocytes which are particularly increased, though at times there is a uniform increase in all varieties of leukocyte. In the dog, on the other hand, the latter condition is found, or there is a leukocytosis due to increase of neutrophilic polynuclear cells. The digestive leukocytosis is not to be considered as a protective reaction of the organism, such as one observes after injection of foreign matters into the body.

Paroxysmal Ventricular Tachysystole of Psychic Origin.—K. KURE (*Deutsch. Arch. f. klin. Med.*, 1912, cvi, 33) reports the study of an eleven year old girl with tachycardia due to ventricular extra-systoles. The attacks were brought on by psychic irritation. Analysis of simultaneous tracings of veins, artery, and heart apex demontrated the fact that the condition was essentially a ventricular tachysystole which was quite independent of auricular rhythm. Whether in this case the ventricular tachsystole was due to heterotopic native impulses in the ventricles or whether it arose through an increase of the irritability (Anspruchsfähigkeit) of a certain part of the ventricle is not clear. It is, nevertheless, highly probable that in this cases the extrasystoles are attributable to stimulation of the accelerans. As a result of the ventricular tachysystole, a complete dissociation was produced temporarily. Kuré suggests that a part of the cases of paroxysmal tachycardia are due to ventricular extrasystoles. [An observation which has been made by many students.—W. S. T.]

The Chemistry of Tuberculous Sputa.—R. EISELT (*Zeitschr. f. klin. Med.*, 1912, lxxv, 71) has studied tuberculous sputa particularly with reference to their enzymatic activities. The methods of examination are described in detail. He finds that the proteolytic enzyme usually

present in tuberculous sputa is a tryptase, but it is by no means so constantly present as has been supposed heretofore. Frequently tryptase alternates with antitryptase in the sputum. Usually this is the case during febrile periods. Like pancreatic trypsin, the tryptase of the sputum, activated with calcium salts, has plastein-forming activity, which is retained in the presence of antitryptase. Lipolytic enzymes were not demonstrable. The proteolytic activity varies inversely with the coagulable protein of the sputum and directly with the quantity of albumoses and amino-acids. Chemical examination of tuberculous sputa showed that of all inflammatory lung diseases tuberculosis is associated with the highest values for coagulable protein. Albumoses are also more abundant than in other diseases. Peptones, on the other hand, are present only in traces; it is probable that they are absorbed almost as rapidly as formed. Of other nitrogenous bodies, the large quantity of incoagulable nitrogen (Rest-N) is striking. It is chiefly in the form of glycosamine and amino-acids.

Adrenalin in Pathological Sera.—STEWART (*Jour. Exper. Med.*, 1912, xv, 547) attempted to demonstrate adrenalin in the sera of blood obtained by venesection from 14 patients suffering with different maladies among which were malignant Graves' disease, myxedema, chronic nephritis, arteriosclerosis, angina pectoris, syphilis, general paresis, gout, and pneumonia. For detection of adrenalin in blood serum Stewart suspended rabbit intestinal and uterine segments in Ringer's solution and measured the increase in the size of the beats and the degree of muscle tone when the medium was replaced by the serum in question. No one of the pathological sera yielded evidence of the presence of adrenalin. This result is explained by Stewart's experimental work. Serum from the adrenal veins of the dog collected with the least possible disturbance gave a negative reaction. Whereas in serum collected during mechanical stimulation of the gland the reaction was distinctly positive. Stimulation of the splanchnics changed a negative reaction to positive in serum of blood from the inferior vena cava, draining the adrenal and lumbar veins. The general admixed blood of the inferior vena cava and elsewhere more distant in the general circulation failed to show the presence of adrenalin whether the splanchnics were stimulated or not. The cause of the negative result is without doubt the high degree of dilution in the inferior vena cava of the blood coming from the adrenals, greater than a dilution of 1 to 1,000,000 as measured by this method.

Malarial Pigment and the Malarial Paroxysm.—BROWN has shown that the pigment elaborated from the hemoglobin of the red blood corpuscle by the malarial parasite and liberated into the circulation of the host at the time of segmentation of the parasite is undoubtedly hematin. In his work upon hematin metobolism he noted that a rabbit receiving an intravenous injection of this pigment developed a very pronounced shaking chill strikingly like that of malaria. With the hope of finding in this substance one of the hypothetical toxins operative in malaria Brown (*Jour. Exper. Med.*, 1912, xv, 579) undertook a series of ninty observations upon the effect of the intravenous injection of alkaline hematin in rabbits. The hematin used was derived

from rabbit, dog, and ox blood, the effect being the same in each instance. After careful previous records of temperature, and observations of the effect of the alkaline medium, the injections in question were made intravenously. Simple calculation on the basis of 4.47 per cent. hematin in hemoglobin and a 1 per cent. (at least) infection of the red blood corpuscles would give 3.7 milligrams of hematin per kilo of body weight as the amount liberated in an average paroxysm of malaria. Brown's dosage was from 1.3 milligrams to 28 milligrams per kilo of body weight, corresponding roughly to an injection of 0.3 to 7.5 per cent. of the red blood corpuscles. Without exception every dose of hematin administered elicited a definite temperature response. Within certain limits the extent of temperature elevation was proportional to the amount of hematin injected. Even other features suggest a malarial paroxysm. After a short period of restiveness the temperature rises and the animal's skin becomes pale, cyanotic, and cold. There is even shivering. This stage of chill lasts an hour and is terminated abruptly by a dilation of the superficial vessels, the ears becoming flushed and hot. This coincides with the initial drop and the duration of temperature above normal. In a word the injection produces a paroxysm characterized by a short prodromal stage, a stage of chill and rise in temperature, and a hot stage, identical in details with the corresponding ones in the paroxysm of human malaria. In the estimate of Brown, the pigment hematin as liberated by the malarial parasite into the circulation of the human host is at least a potentially toxic substance.

Albuminuria and Cylindruria.— BARRINGER and WARREN (*Arch. Int. Med.*, 1912, ix, 657) have studied the question of the significance of albumin and casts in the urine of apparently healthy men. The material at their disposal were the records of 396 men examined for life insurance ten years before. As far as ordinary physical examination could determine, they were normal at that time except for the presence in the urine of serum albumin with or without casts. They were divided into three groups, as follows: 115 showed simple albuminuria; 203, albuminuria and a few hyaline casts; 53, albuminuria and a few granular casts. The incidence of albumin and of granular casts increased with each decade, but the decade-incidence of the hyaline-cast groups was almost equal. Ten years after these records, 70 of the orginal list were visited and examined. No one of 20 in the group of simple albuminuria had interstitial nephritis. In 8 the same condition persisted, 30 of the men had showed albumin with hyaline casts. One of these had developed nephritis, in comparison to 2 of the group with albumin and granular casts. Two in the second group and 5 in the third were doubtful. In the entire series of 70 men, 38 were free from cardiac or renal disease. Three surely and 7 possibly have chronic interstitial nephritis, 22 still show the same urinary condition as they did ten years ago. The mortality of the original group was decidedly high, 25 instead 16 as it would have been computed for men free of albumin and otherwise normal. The absence of nephritis shown in the 20 cases of simple albuminuria, after ten years, and the low mortality in this group from renal and arterial disease indicate that it is exceptional for the albuminuria of young adults to become a symptom of incipient nephritis.

SURGERY

UNDER THE CHARGE OF

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The Influence of an Aseptic Serous Inflammation upon the Dissolution of Catgut.—CALLAM (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 265) says that an aseptic serous inflammation delays the dissolution of catgut in the mouse, an animal which absorbs the thread very quickly in the presence of severe suppuration. In the cases where the reaction on the inserted catgut is slight, as in the guinea-pig, no effect could be shown. The results of his experiments show that an artificial inflammation delays the absorption of catgut in the body of the white mouse. The uninfluenced process is nothing more than an aseptic suppuration. This process is moderated because the edema, caused by the artificial aseptic inflammation, scatters the leukocytes and permits only a slow development of their contained digestive strength. The tissues, therefore, which are subjected to the peptic influence, as well as the catgut, undergo less damage. Callam, in this way, coincides with the view of Bier, that the inflammation and its inherent healing power serve to moderate the damage done by the exciting cause of the inflammation. Since, as Joseph says in his text-book on hyperemia treatment, the slower and more mild the abnormal chemical process set up by the inflammation, attacks the surrounding tissue, the more time the tissue has to guard itself against the hurtful influence and to prevent the threatened field from damage and destruction. The flames which scorch the flesh of the unfortunate one in a few moments, allows the body no defence. So with the summer sun, which burns the body during weeks and months. The bacterial inflammations act in a similar manner. We have here a scientific explanation for the fact, discovered empirically, that catgut impregnated with antiseptics are destroyed more slowly than the catgut without antiseptic impregnation. When the inflammatory irritation does not cause edema of the tissues in which the catgut lies, the aseptic leukocytosis can develop more quickly and digest the catgut and tissues.

An Experimental Contribution Concerning the Formation of Bone from the Injection or Implantation of Periosteum Emulsion.—JOKOI (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 433), following the work of Nakahara and Dilger in the production of bone formation, carried out their experiments, chiefly on rabbits, rarely on dogs. They

removed periosteum from the tibia and with sharp instruments divided it into small pieces. These were implanted subcutaneously or in the muscles. After varying periods they were cut out of the tissues and examined. From autoplastic implantation or injection of periosteum emulsion, Jokoi could, in 6 out of 7 experiments, produce a more or less marked bone formation. The active bone formation depends, above all, upon the mechanical relations of the implanted or injected pieces of periosteum to the surrounding tissues. In the unsuccessful experiments these were always shrivelled up or rolled together. In one of the experiments he established that the new-formed piece of bone had not undergone any absorption, but had shown rather a tendency to wider extension. From homoioplastic implantation or injection of periosteum emulsion also, bone formation can be produced, although not so frequently or so markedly as from the autoplastic. From heteroplastic implantation or injection of periosteum emulsion, no bone formation could be produced. The associated injection of fresh blood of the same animal appeared to have no favorable influence upon the osteoblastic activity of the transplanted pieces of periosteum. In all the experiments the associated particles of bone underwent lacunar absorption.

Small Plastic Operations on the Fingers and Hands.—KLAPP (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 479) reports several ingenious operations to make the hand more useful after injuries. When a finger has been cut off and the cut surface is even, it has usually been necessary to remove a piece of the phalanx in order that the end of the bone could be covered by the skin and underlying soft tissues. This sacrifices some of the length of the finger and increases the loss of function seriously, particularly in certain occupations, as in physicians and piano players. In one case in which the end of a finger had been cut off obliquely at the level of the middle of the finger-nail, a palmar flap having a lateral attachment was made and carried over the end of the bone, its free end being sutured in place on the opposite side of the finger. When the cut is transverse, by a transverse incision on the palmar side a short distance from the cut margin of skin, a flap can be made which is attached on both sides. This can be drawn by sutures as a bridge of tissue over the end of the bone. In a case in which the thumb was entirely removed, even with the side of the hand, Klapp separated the metacarpal bone of the thumb from the rest of the hand by dividing the soft tissues between. Two skin flaps were formed, one from the palmar and the other from the dorsal side. The interossei muscles were then divided, and one skin flap was used to cover the raw surface on the thumb side, while the other flap was made to cover the raw surface on the hand side. In this way the patient was given a short but very useful stump for a thumb. An illustration shows the repaired had grasping the handle of a mallet, the improvised stump of the thumb seeming to add much to the firmness of the grasp.

The Clinical Utilization of the Coagulation Time of the Blood in Jaundice.—KUNIKA (*Deutsch. Zeitsch. f. Chir.*, 1912, cxviii, 574) says that the taking of the coagulation time of the blood is rarely used in practical medicine because the methods thus far employed are not

easily carried out. He believes the Kottmann method is easy of performance and very reliable. In many patients jaundiced from gallstone disease, the clotting time is normal, and there is no inclination to hemorrhage. In very grave cases of jaundice in which there is a tendency to hemorrhage, the ability of the blood to clot is very much lowered. This is independent of the intensity of the jaundice. When in patients with jaundice, who come for operation, an examination shows a retarded clotting time of the blood, we may assume the existence of an advanced stage of a liver affection, which renders the case no longer suitable for operation. The examination of the coagulation time of the blood has a diagnostic and prognostic value for the practical physician, and especially for the surgeon, since it permits him to avoid a dangerous operation. It is also an important aid for the differential diagnosis of jaundice.

The Surgery of the Deep Pelvic Lymph Nodes.—KOTZULLA (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 55) says that the surgery of the deep pelvic nodes is concerned chiefly with malignant degeneration and tuberculosis. In malignant disease we can limit the extirpation to the inguinal region only in the beginning of the disease. In every other case, that is, whenever there is only a slight suspicion that the disease has already advanced, it becomes necessary to lay open the femoral canal, and after dividing Poupart's ligament to investigate the suprafemoral nodes. If these are diseased we should proceed further. In tuberculosis a radical procedure is also necessary. In general an excision of the superficial nodes should be done only when the disease is actually limited to these, in all other cases a radical operation being necessary. It is to be admitted that an undiscriminating search for the deep pelvic nodes is to be avoided, in view of the considerable danger of lymph stasis and chronic edema of the extremity. In the absence of contraindications, the exposure should include the suprafemoral or deeper nodes. The chief contraindications will be: The existence of generalized tuberculosis, the simultaneous existence of disease of vital organs, and the invasion of the more centrally located groups of nodes which are not surgically accessible. The age and general condition of the patient are also to be considered. The operation of choice is that of Sprengel. He extirpates the usually diseased inguinal nodes by means of a longitudinal incision, and lays the femoral vessels free to Poupart's ligament. In order to have a free exposure and to command the anatomy of this region so as to avoid untoward accidents, the ligament is divided opposite the vessels. By an oblique incision along Poupart's ligament the reflection of the peritoneum is exposed. By elevation of the pelvis the peritoneum is carried backward so that the nodes and large vessels are exposed. Now follows the extirpation of the nodes under continuous control of the vessels up to the bifurcation of the common iliac vessels. The wound is partially closed by sutures and the rest by gauze packing. The prognosis of the operation is relatively favorable. While it is extensive the shock produced by it is relatively slight. None of the patients died during or at the end of the operation. The further prognosis, especially in malignant disease, depends naturally upon the extent of the disease. The cases which are in the beginning stages

of the disease promise a good permanent result. If, however, the deep pelvic nodes are already involved to a considerable degree, the prognosis will vary with the grade of the disease. Such cases will probably be excluded ultimately from those suitable for operation. The prognosis in tuberculosis is generally favorable.

Statistical Contribution Concerning the Result of the Wilms Method of Treating the Stump in Resection of the Stomach.—KUNIKA (*Deutsch. Zeitsch. f. Chir.*, 1912, cxix, 483) describes the technique as follows: A median incision is made, beginning at the xyphoid cartilage. The pyloric portion of the stomach is brought forward as far as possible, and the extent of the tumor, the lymph-node involvement, and the adhesions are established. The gastrocolic ligament is now divided, after double ligature of its vessels. The nodes in the gastrocolic ligament remain attached to the stomach. The separation will be carried in the direction of the duodenum as far as the enlarged nodes extend, or otherwise a thumb's breadth beyond the tumor. The upper portion of the duodenum is also isolated on all sides. The lesser omentum is divided beyond the palpably enlarged nodes between clamps or ligatures. The exposure must extend considerably further on the cardiac side than on the duodenal. Then follows the division of the duodenum. A strong closing suture is applied in the pressure groove made in the duodenal stump by the clamp, and is tied. This with the stump is inverted by one or two purse-string sutures. After the turning in of the stump the ligature closing it is removed. The gastric stump will then be closed in its upper half down to the opening left for anastomosis, which will be united to one in a coil of the jejunum passed through an opening in the mesocolon. The wall of the small intestine at the anastomosis is made to cover some of the sutures closing the divided end of the stomach for a short distance above the anastomotic opening. This strengthens the weakest place in the anastomosis. The afferent limb of the anastomosed loop of the jejunum is fixed to the margins of the opening in the mesocolon by several sutures to prevent later ileus from the passing through the opening of another coil of intestine. After the usual cleansing of the field of operation, and covering of the sutures with omentum, the abdominal wound is closed in layers in the usual way. Fourteen cases operated on in this way by Wilms are reported. All but one left the hospital well, this one dying of an intercurrent pneumonia.

A Study of Vesico-intestinal Fistulæ.—PRISTAVESCO (*Jour. d'Urol.*, 1912, ii, 321) says that acquired vesico-intestinal fistulæ constitute a rare affection. They can be divided into three catagories, according to the segment of the digestive tube in communication with the bladder and according to their characteristics: (1) Those between the bladder and the rectum, and large intestine in general. (2) Those communicating with the acquired intestinal diverticula with a predilection for the sigmoid colon. (3) Those communicating with the appendix, ileum, or colon. Of the three kinds, the diverticulo-vesical fistulæ are the most rare, their proportion being about 2 per cent. All varieties have their origin in common causes, that is, they may be due to trauma, inflammation, cancer, and tuberculosis. More

rarely they may be due to actinomycosis or syphilis. The symptoms, aside from those of the causal affection, are the emission of gas, fecal matter, or alimentary debris by the urethra, and the escape of urine by the anus. Later are added those of secondary infection, and the constitutional symptoms. The diagnosis of recto-vesical fistula is made by the recognition, by the rectal touch or rectoscopy, of the fistulous orifice. The diagnosis of the appendiculo-vesical variety is made more certain or probable when it is preceded by an appendicitis. The diverticulo-vesical can only be suspected in patients suffering from disease of the heart or liver with edema, and in those in whom one establishes a painful swelling in the left iliac fossa. One can only make conjecture as to whether the abnormal communication is direct or indirect. In the female it is nearly always indirect. The prognosis of vesico-intestinal fistulæ is grave. The average duration of life, according to Pascal, is three years. The treatment should be preventive in the cases in which the fistula is threatened, and it is directed to the diseased organs (bladder, intestine, or neighboring organs) to guard against the fistula formation. The treatment will be palliative in inoperable cases (tuberculosis, cancer, etc.). Medical treatment, local, and general, should always be employed in cases of vesico-intestinal fistula to prevent infection along the ureter to the pelvis and kidney. It will be preparatory to operation and will aid in the cure of cases operated on. The surgical treatment consists in the removal of the abnormal communication. For this purpose several paths have been tried, but the best, according to the results obtained, appear to be the peritoneal and transvesical.

Treatment of Dislocation of the Head of the Radius Complicated by Fracture of the Ulna.—Ashhurst (*Annals of Surgery*, 1912, lvi, 631) says that in recent cases reduction of the dislocated radial head should be secured, by arthrotomy and capsulorrhaphy if necessary. As Kirmissen says, in such injuries the dislocation is everything, the fracture nothing. When reduction is secured the fracture almost invariably falls into good position. If it does not, it may be fixed by suture or plate. In old cases with the ulna united, attempt reduction of the dislocation by arthrotomy, and retain the radius in place by capsulorrhaphy. If reduction after arthrotomy proves impossible, as it may if the ulna has united in bad position, it is better to excise the head of the radius than to interfere with the ulna, unless the deformity in the ulna is extreme. In such cases osteotomy of the ulna may be done. In old cases with non-union of the ulna, expose the ulna fracture first, and after freeing the fragments, secure reduction of the dislocation (by arthrotomy if necessary, including capsulorrhaphy); then treat the ulnar fracture as if no dislocation had existed. In cases with musculospiral paralysis, excision of the radial head failed to secure a good result in 1 case (Zschock), and there is no evidence that reduction and capsulorrhaphy would not have been successful in two others (Albertin, Kammerer) in which excision was done.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Syphilis with Neosalvarsan.—WOLFF and MULZER (*Münch. med. Woch.*, 1912, lix, 1706) report their results with the use of neosalvarsan in 30 cases of syphilis. They conclude that neosalvarsan is far less powerful than salvarsan as a specific for syphilis even when used in larger quantities, and that it is far more dangerous. They warn particularly against its use in ambulant patients. The toxic effects observed were as follows: A chill in 1 case; Herxheimer's reaction in 3 cases; headache, vomiting, and diarrhea in 14 cases; extensive drug eruptions in 4 cases; herpes labialis in 2 cases; nephritis, paralysis, and other severe symptoms in 1 case.

Experiences with Neosalvarsan.—KALL (*Münch. med. Woch.*, 1912, lix, 1714), upon the basis of 39 cases of syphilis treated with neosalvarsan, warns against frequent repetitions of injections because he observed severe toxic effects following the use of neosalvarsan in this way. He also condemns the recommendation that ambulant patients be treated with neosalvarsan.

The Treatment of Gout with Atophan.—BACH and STRAUSS (*Münch. med. Woch.*, 1912, lix, 1714) report 19 cases of gout treated with atophan in doses of 0.5 gram combined with sodium bicarbonate, 5 grams, at four-hour intervals for three-day periods. These periods of atophan treatment were followed in every instance by an increased uric acid excretion to double that existing before the treatment. Usually the increase in the uric acid was noted on the first day of the administration of atophan. The withdrawal of the remedy was followed by a decline of the uric acid excretion below the normal that slowly rose to its former level. The administration of the remedy gave rise to no kidney irritation and no increase in the amount of the urine. In fact 2 patients with contracted kidneys bore atophan without any untoward symptoms and with no change in the urinary findings regarding albumin and casts.

The Treatment of Diphtheria Carriers by Overriding with Staphylococcus Aureus.—LORENZ and RAVENEL (*Jour. Amer. Med. Assoc.*, 1912, lix, 690) report their results with reference to ridding the throats of diphtheria bacilli by means of a staphylococcus aureus spray. In all 17 patients received this form of treatment. Three were carriers, pure and simple, never having shown local or general symptoms of diphtheria. Six patients had clinical symptoms of diphtheria, but persisted as carriers long after convalescence had been established.

In 8 cases the staphylococcus spray was used early in the course of the diphtheria. The preparation used was a fresh suspension of the Staphylococcus pyogenes aureus in normal saline solution or a bouillon culture twelve hours old. The spray was given at a temperature of 96° F. Sufficient was used to make the pharynx "dripping wet" and the nasal cavities were sprayed until the liquid ran down the back of the throat. They advise a combined nasal and throat spray, to be given at four-hour intervals on two succeeding days; the first swab for examination should be made the third day. The best results were obtained in the diphtheria bacillus carriers. In 2 cases negative reports were received after six applications of the spray, and in the third after nine applications. Four other cases cleared up within one week, but on the other hand one required six weeks and another fifty days of treatment before the throat was freed of diphtheria bacilli. Lorenz and Ravenel believe that in those cases where the spray was used early in the course of the disease, better results were obtained in those patients treated with the staphylococcus spray than in those treated by the ordinary antiseptic applications.

Vaccination for Typhoid by Living Sensibilized Bacilli Typhosi.—Broughton-Alcock (*Lancet*, 1912, clxxxiii, 504) draws the following conclusions from his observations as to the effect of vaccination with sensibilized typhoid bacilli. (1) The successful experiments on man by the method of Besredka have taken us one step forward in the application of vaccination. Cannot the sensibilized living Bacillus typhosus be considered in the same light as the virus of smallpox, attenuated or modified by the immunized calf-lymph, and which gives rise to a specific immunity that may be verily called ideal? (2) The sensibilized living bacilli remain alive over four months without exceptional precautions, and their preparation is simple, rapid, and practical. (3) The first dose for a woman of average size should be 500,000,000 sensibilized living bacilli in 1 c.c. of 0.8 per cent. saline. For a man of good physique the first dose should be 750,000,000 in 1 c.c. of 0.8 per cent. saline. The second dose, seven to nine days later, should be double these quantities. The dose of 500,000,000 represents 1 c.c. of a culture of twenty-four hours on gelose without peptone in 100 c.c. of saline. Diluted 1 to 40 and at the dose of 0.1 c.c. it fixes 0.1 c.c. of titrated guinea-pigs complement. (4) There is no general reaction and only an insignificant local reaction following these injections. The patient is in no way obliged to change his daily routine of living. These results are in marked contrast with Broughton-Alcock's experience of the reactions following the injections of the same number of killed bacilli in the vaccine of Wright-Leishman. An elevated temperature, a previous history of typhoid, and the time of menstruation are not contraindications to the giving of the living sensibilized Bacilli typhosi. (6) The sera of persons injected with sensibilized Bacilli typhosi have not been found to deviate complement and only rarely to agglutinate an emulsion of a young culture. Their addition, however, markedly increases phagocytosis. Probably they also contain anti-endotoxin bodies. (7) The detected presence of specific amboceptors, agglutinins, bacteriolysins, cannot be said to show the degree

of immunity attained. The results of experiments in vitro cannot be interpreted as denoting the state of the patient's resistance. (8) As it has been asserted by all authors that vaccination by living microorganisms is the most effective, and, moreover, this has been proved by the experiments on chimpanzees made by Metchnikoff and Besredka, and as Broughton-Alcock's observations on man have proved the innocuousness of the living sensibilized Bacillus typhosus, he presumes to conclude that this method ought by preference to be applied to man. Since the writing of this article 750 persons, including many soldiers, have been inoculated. The results are most satisfactory and encouraging.

Hexamethylenamin in the Treatment of Systemic Infections, with a Special Emphasis upon its Use as a Prophylactic.—Crowe (*Johns Hopkins Hospital Bull.*, 1912, xxiii, 255) says that the suggestion that hexamethylenamin be used in the treatment of systemic infections is based entirely upon the results of experimental and clinical observations. He believes that it is of value not only as a therapeutic, but especially as a prophylactic measure in a great variety of maladies. Among the conditions which may be favorably influenced by the administration of hexamethylenamin the following are the most important: (1) Infections of the genito-urinary tract and typhoid bacilluria; (2) infections of the bile-ducts and gall-bladder; (3) infections of the cerebrospinal system, poliomyelitis, epidemic meningitis, meningeal infections following injuries or infectious processes elsewhere in the body; (4) infections of the respiratory tract, including infections of the paranasal sinuses and ears, acute rhinitis, acute tonsillitis, and some forms of bronchitis. In lobar pneumonia and pulmonary tuberculosis it is doubtful whether this drug is of any value. Hexamethylenamin, given either by mouth or by rectum, makes its appearance in the bile and in the urine almost simultaneously. Provided large doses of hexamethylenamin are given, at least 75 grains a day, this drug appears in the gall-bladder in a concentration which suffices to render the bile an unsuitable media for the growth of bacteria. Since 1908 it has been a routine measure in the Johns Hopkins Hospital to administer hexamethylenamin in all cases in which a meningeal infection is a possible or threatened complication. There have been 20 cases of compound fracture of the vault, similar in that there was a laceration of the meninges and underlying cortex in each instance. In 8 of the earlier cases hexamethylenamin was not given, and the mortality from infection was 50 per cent. To each of the remaining 12 cases, hexamethylenamin was given immediately after the injury, and at frequent intervals, until all danger of infection was past. Ten of these patients recovered, while 2 succumbed with a pneumococcal meningitis. In 40 cases of hypophysis tumor operated upon, hexamethylenamin has been administered as a prophylactic measure. It was given in doses of from 40 to 60 grains during the twenty-four hours preceding the operation, and even larger amounts for several days after the operation. In 31 cases there were no postoperative complications whatever. In 9 cases there were symptoms suggesting a meningeal infection. Three of these patients finally succumbed to

meningitis; the other 6 patients recovered. They have abandoned the custom of giving this drug in doses of 10 to 15 grains at stated intervals, since it is often difficult to induce the patient to take the 250 or 300 c.c. of water in which doses of this amount should always be dissolved. In very ill patients, the drug is usually administered by rectum, from 50 to 100 grains being dissolved in a liter of salt solution, and allowed to flow into the bowel a drop at a time. There has not been the slightest evidence of undue irritation of the intestinal mucosa, even after one or two weeks of almost continuous administration by this method. If the patient is able to take nourishment by mouth, from 2 to 3 grains of hexamethylenamin are added to every ounce of liquid, and it is often possible in this way to give from 60 to 100 grains a day without the patient's knowledge and without producing gastric or renal irritation. There have been but very few instances in which toxic symptoms have resulted from the administration of large doses of hexamethylenamin, although from 200 to 300 grains daily for four or five days were given; even in children, doses of 100 or 125 grains a day have produced no irritative symptoms. In 95 cases in which the average dose of hexamethylenamin was 75 grains a day for ten days, painful micturition and hematuria occurred in 7 instances. Three of these cases were fatal meningeal infections, and the drug was given in unusually large amounts with the hope of checking the progress of the disease. At the post mortem examination it was apparent that the hematuria had its origin from the mucous membrane of the bladder, and was not due to an acute renal irritation. In the remaining 4 cases the urine rapidly became normal on the withdrawal of the drug. Crowe says that in a few persons very susceptible to the drug, even a small dose may give rise to skin rashes, catarrh of the mucous membranes, gastric or urinary irritation. However, this fact does not invalidate the use of the drug. He believes that untoward symptoms usually arise as a result of insufficient dilution, and such symptoms have invariably disappeared on withdrawing the drug and producing active diuresis by forcing liquids.

The Crotalin Treatment of Epilepsy.—SPANGLER (*New York Med. Jour.*, 1912, xcvi, 520) adds to previous communications on this same subject. Since first using the venom in the treatment of epilepsy (March, 1909), he has used it in 109 cases, and has given to these patients over 2000 injections of the venom without untoward effects. He gives a *resume* of the results in 6 of the 11 cases first reported that he has since kept under observation. Five of these patients have been free from convulsions for periods of from seventeen months to three years and three months. One patient who formerly had from two to five major convulsions each week now only has one attack every three or four months, and physically and mentally has made such improvement that he can work regularly at his employment. Crotalin solution is made from the dried, yellowish crystal-like scales of the evaporated venom of crotalus horridus, the rattlesnake. The venom is obtained from the living reptile and dried between glass plates, under a bell jar, in the sun. The crystals are dissolved in glycerin and sterile water, to which a few drops of tricresol are added as a preservative. The solution is standardized and given by hypodermic injection. Spangler

believes that the venom treatment is indicated in many of the essential cases of epilepsy. He says that not only are the virulence and number of epileptic convulsions favorably influenced by the crotalin treatment, but the excitability of the nervous system is modified and the general health of the patients, their mental facilities, and metabolism in every respect are considerably improved. The quality of the blood, and possibly its chemical composition seem to be affected by the injection of the venom. As to the exact effect it has on the coagulability of the blood, further observation is necessary. There is no danger in the use of crotalin as long as the necessary aseptic precautions are taken in its administration and the treatment is carried out with careful observation as to its effect on the patient.

Further Experiences of the Specific Curative Action in Amebic Dysentery of Hypodermic Injections of Soluble Salts of Emetin.—ROGERS (*British Med. Jour.*, 1912, 2695, 405) believes that emetin salts administered hypodermically in sufficient doses will kill amebæ in both the intestinal and liver abscess walls. With regard to dosage he says that either the hydrochloride or the hydrobromid of emetin are equally useful, the former being the more soluble, while the latter requires about 2 c.c. of sterile water or saline to dissolve it. At first Rogers chiefly used $\frac{1}{3}$ grain doses, but now very seldom employs less than $\frac{1}{2}$ grain at a time, and often gives as much as $\frac{2}{3}$, the equivalent of 60 grains of ipecacuanha, and has twice injected 1-grain doses subcutaneously without any vomiting or depression, but such a quantity is only required in extremely acute amebic dysentery. Rogers says that the extraordinary rapidity with which marked improvement follows the subcutaneous injections of $\frac{1}{2}$-grain doses of emetin is of the greatest diagnostic importance for cases of bacillary dysentery, and that other non-amebic causes of the presence of blood and mucus in the stools are not materially affected by the drug, although it has done no harm in them. In Rogers' experience, whenever active amebæ of the histolytica type, including the variety described by Noc and shown by Greig to be the common one in India, have been found in dysenteric stools, the disease has eventually proved amenable to full doses of ipecacuanha, if not too acute or far advanced. Rogers gives details of a few cases of amebic dysentery and amebic abscesses of liver and spleen treated by this method with good results.

PEDIATRICS

UNDER THE CHARGE OF

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OF PHILADELPHIA.

Serous Meningitis and Associated Conditions in Childhood.—KURT BLÜHDORN (*Berlin. klin. Woch.*, 1912, xlix, 1796) reports a study of 11 cases of serous meningitis. This term is used to designate the

external form of the disease in which there is an increase of fluid in the subarachnoid space, due to an inflammation of infectious origin. A serous meningitis can be caused by the typhoid bacillus, the pneumococcus, the bacillus of influenza, the meningococcus, and especially by the streptococcus originating in the ear. While a serous meningitis may be merely the fore-runner of a purulent meningitis, and may cause death in the first instance without apparent pathological change in the tissues, yet there do occur pure cases of serous meningitis in which the fluid remains clear and these cases almost invariably recover. Blühdorn believes that in some cases the substances elaborated by the bacteria, through chemical action on the brain cells and surrounding tissue, excite the plexus to hypersecretion. Independently of primary serous meningitis, there occur similar meningeal conditions during pneumonia and pertussis in which no bacteria can be found in the spinal fluid by the most careful bacteriological tests, both cultural and animal. Therefore, it is assumed that this specific factor of the primary disease or its toxin is the etiological factor of the meningitis. Blühdorn's cases all showed the general symptoms and course of a meningitis with an increased quantity of clear spinal fluid under pressure of more than 12 to 15 cm., which in children can be considered pathological. The result of the lumbar puncture showed invariably an absence or at most a slight trace of albumin, very few formed elements when present at all, and no bacteria under the most careful tests. Rigidity of the neck and Kernig's sign in children aged under three years are difficult to determine, as is also the bulging of the fontanelles. Three cases of serous meningitis were associated with a pneumonia. One of these cases ultimately developed pus in the spinal fluid which showed also the pneumococcus. The other 2 cases remained clear types of serous meningitis undoubtedly actuated by the bacterial toxins only. Two cases of serous meningitis developed during pertussis, where the actuating factor may have been either the pneumococcus or the specific organism of pertussis. Five cases are discussed in which there was no primary disease present to explain the meningitis and in which the spinal fluid was sterile although under high pressure, and at times showed a trace of albumin and a few lymphocytes. Lumbar puncture in many of those cases had a beneficial effect on the acute condition, although several cases subsequently showed mental impairment.

Icterus Simplex in Childhood.—Albert Niemann (*Med. Klin.*, 1912, viii, 1624) prefers the name icterus simplex because no proof of an infectious etiological factor has appeared, although the onset and course of the disease gives one the impression of an infectious condition. Icterus simplex is common in childhood, and several observers have reported from 50 to 73 per cent. of cases as occurring in children during a general outbreak of the condition. In Berlin, however, the average occurrence in children seems to be 1 per cent. of all cases of icterus. Niemann bases his article on a series of 130 cases. The majority of cases follow a mild type, clinically, with a short duration of about one week and usually no symptoms, except the icterus of the skin and sclera, and icteric urine. Occasionally there occur anorexia, coated tongue, or vomiting. The feces are usually normal. The

other type of cse exhibits prodromal-like symptoms of fever, headache dizziness, chills, anorexia, nausea, and vomiting. This type of attack simulates more closely a general infection, especially since a number of days elapse before the appearance of icterus, and, as a rule, the gastro-intestinal symptoms do not develop. Enlargement of the liver was a rather frequent symptom in this series, but disappeared with the fading of the icterus. A slowing of the pulse was rarely observed. In a very small group of cases the disease was protracted over weeks or even months. In this class the gastro-intestinal symptoms were especially marked, the icterus more intense and lasting, and the liver was swollen to a marked degree. Practically all authorities agree that this condition is found most prevalent in the fall months and many observers refer to epidemics of this disease in the Fall. In Niemann's cases 55 per cent. occurred in the months of October and November. This fact, with the occurrence of a number of cases in the same family, especially among sisters, is an argument in favor of an infectious etiological factor. The disease rarely affects children aged under two years, and the greatest number of cases occurred between the seventh and eighth year. Niemann found a fat-free diet unnecessary, of no therapeutic value, and accompanied by marked loss of weight. A moderately fat diet had no ill effect on the icterus and kept the children in a better-nourished condition.

The Practical Significance of Uniformly Deep Rectal Temperature Measurements in a Child.—PAUL TACHAN (*Münch. med. Woch.*, 1912, lix, 2101) conducted 300 double measurements of the rectal temperature in 30 children in an attempt to explain the variations in the rectal temperature so often found in children, without demonstrable cause. Feer had previously indicated that the cause was often found in the variation in the depth to which the thermometer is placed in the rectum, at different times. In each trial the thermometer was inserted only to the end of the mercury bulb and kept there until the mercury remained constant; it was then inserted deeply, about 5 cm., until the mercury remained constant. In this manner ten different measurements were taken on the same child. It was found that between superficial measurement and deep measurement there existed a difference in temperature of between 0.1° and 1.7° or on an average of 0.5.° As a rule, in only a few children did the curve of the superficial reading and the deep reading run quite parallel. More often the temperature difference varied in the same child on different days. Sometimes the superficial curve was very irregular, while the deep curve remained fairly constant. Explanation of the causes of these differences in children was not found. During a fever the difference between the two curves becomes less, but after the temperature has fallen it becomes greater again. Several cases showed an increasingly greater difference after each temperature fall, following a recurring fever, but always approximating again with each new attack of fever. While this investigation may not indicate any new discoveries, it is sufficient to show that in taking rectal temperatures the thermometer should be placed as deeply as possible, and always at the same depth in the rectum.

The Diagnosis of Tuberculosis of the Lungs in Children.—Hans Vogt (*Münch. med. Woch.*, 1912, lix, 1957), in this article, selects certain points in tuberculosis of the lung in children which permit of frequent errors in diagnosis. The severe forms of the exudative diathesis have been formerly held to be scrofulous, but Czerny has unmistakably proved that the symptoms of this condition may arise in early infancy, unassociated with tuberculosis, and showing a negative cutaneous tuberculin reaction. Temperature elevation in children where all apparent causes can be eliminated, should not necessarily be put down to a tuberculous infection. In children an increase in temperature occurs frequently over quite a period of time, due to slight infection of the nasopharynx, or even to psychical disturbances. The tuberculin reaction, while a valuable aid in diagnosis, is capable of being misinterpreted. Distinction must be made between an infection by tubercle bacilli and an actual tuberculous process in the body. It is only within very narrow limits that the tuberculous reaction can be applied in a diagnosis of an active process, as in infancy where almost every infection by the bacilli, leads to a progressive tuberculosis. Chronic bronchitis in children is sometimes taken for tuberculosis. From the second to the tenth year Vogt finds as large a proportion of the one as of the other. Especially in case of recurring pneumonia with later areas of circumscribed infiltration and a diffuse bronchitis with occasional exacerbations, is a diagnosis of tuberculosis erroneously made. It rarely occurs that an acute tuberculosis process in the lung will have periods of quiescence, whereas this feature is characteristic of a chronic bronchiectasis.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Ectopic Gestation.—Cragin (*Surg., Gynec., and Obstet.*, March, 1912) believes that so soon as a diagnosis of unruptured ectopic gestation is positively made, but one method of treatment is permissible—the removal of the pregnant tube by operation. At the time of tubal rupture or abortion, operation is indicated; but some question may arise as to the propriety of operating immediately, or of giving the patient time to recover from shock. Cragin in these cases proceeds as follows: If the patient is seen at the time of a tubal rupture or abortion, operate as soon as careful preparation can be made, unless the patient is in such extreme shock that the operation would probably prove fatal. In this case, watch the patient carefully to see if she is improving or losing ground. If she is improving, operate when the patient is in better condition. If failing, operate rapidly at once, checking hemorrhage with the least manipulation, having an

assistant transfuse, and leaving warm salt solution in the abdomen. Operation should be from above. Two vessels supply the field of operation—the ovarian and uterine—and both should be controlled by a ligature or clamp about the tube, near the uterine cornu and about the upper portion of the infundibulopelvic ligament. The location of these vessels should be kept in mind, and valuable time should not be lost in sponging away blood. The operator should first determine on which side the gestation sac lies, and check hemorrhage as rapidly as possible. As regards the affected tube, it should be removed. If the opposite tube be healthy, this should be allowed to remain. The larger blood clots may be removed by the hands, the smaller may be flushed out by salt solution. The abdomen should be closed without drainage. In interstitial pregnancy, in the majority of cases it is safer to remove the uterus. Occasionally one may excise the affected uterine cornu, leaving the remainder. In intraligamentous rupture and the hemorrhage extraperitoneal and encapsulated, operation may be postponed, with the patient under close observation. Rest in bed, and an ice-bag upon the lower abdomen may check hemorrhage and hasten absorption. If hemorrhage recurs the abdomen should be opened and the source of bleeding controlled. When a pelvic hematoma suppurates, vaginal incision and drainage is the operation of choice. In cases of early ectopic gestation which have ruptured or aborted some time before they are seen, it is usually best to perform abdominal section, removing the tube, blood-clots, and the product of gestation. If suppuration has occurred, vaginal incision and drainage are indicated. In the majority of cases giving a history of tubal pregnancy some time previously, it is best to operate. In a few, where there is no evidence that hemorrhage has recurred, and the tube is empty, and the hematocele diminishing in size, operation may be declined. In advanced ectopic gestation at six months or more, Cragin has operated four times, saving 2 of the children, 1 of whom had congenital dislocation of the hip, but was otherwise healthy. It is best to anticipate spurious labor by operating at eight and one-half months. In dealing with the placenta in these cases, unless the vessels supplying the sac can be ligated and the sac removed entire, the placenta should be left and allowed to separate and come away gradually. Where rupture has occurred downward through the floor of the tube, and the development was intraligamentous, the peritoneum may be raised from the floor of the pelvis and the sac can best be opened by incision at the outer border of the rectus muscle, thus avoiding opening the general peritoneal cavity. The vessels supplying the placenta can often be successfully ligated in these cases, and the sac removed. The abdominal wound may then be closed, and the period of convalescence greatly shortened. Under ordinary circumstances the safest course is to incise the gestation sac, remove the child, stitch the sac to the abdominal wound, and pack the sac with gauze. This should be changed every second or third day, and the separation of the placenta aided with the fingers. The sinus which remains will close in a reasonable time. If the fetus has died some time before operation, and the sac is not infected, the placenta can usually be removed entire. In advanced ectopic gestation, where the fetus has just died, operation may be postponed from four

to six weeks so as to allow the obliteration of bloodvessels. The patient should be under observation, and if evidence of infection occurs, operation should be at once performed. In the presence of infection vaginal section is indicated for drainage; but in the absence of infection the abdominal route is best. If the uterus is found thoroughly adherent to the gestation sac, hysterectomy should be done In prophylaxis, in cases where it is necessary to remove an ovary, the tube on that side should also be removed, as its presence exposes the patient to the danger of ectopic gestation. In the *Amer. Jour. Obstet.*, April, 1912, JELLINGHAUS reports a case of true, ligamentous, unruptured tubal pregnancy at eight months, treated by abdominal section, with the removal of the gestation sac and placenta and membranes. Five days after operation, vaginal and abdominal fistulæ appeared, and on the tenth day a urinary fistula. At the end of the third week fecal and urinary discharges through the vagina had ceased, but continued through the abdominal opening. This closed by the end of the seventh week. Sixteen weeks after operation the patient felt well, but had watery stools, probably from an intra-abdominal fistula. Markol also reports a case of interstitial pregnancy admitted to hospital five years previously, with what was believed to be an incomplete abortion. Curetting was done but no fetus discovered. The patient left the hospital against advice, returning in a few days in collapse, with rapid pulse and high fever. Her condition precluded operation, but she gradually improved under conservative treatment, and left the hospital. She afterward returned stating that she had been delivered by forceps of a very large child stillborn. Bimanual examination showed a tumor on the right side of the uterus extremely tender, and slightly movable. At operation the tumor was directly connected with the right horn of the uterus. The left tube and ovary were enlarged and bound down by adhesions, and were removed. The appendix and the upper portion of the uterus were also removed. The case was probably one of ruptured ectopic pregnancy, five years previously, with subsequent normal pregnancy, followed by interstitial gestation.

Normal Human Blood Serum in the Disorders of the Newborn.—WELCH (*Amer. Jour. Obstet.*, April, 1912) reports the case of a premature infant at eight months, taking nourishment badly, and steadily losing weight. Subcutaneous injections of normal human serum, from 20 to 78 c.c., a total of 896 c.c. in twenty-one days, were given with some benefit. The child improved and was able to nurse well. In 32 cases of newborn infants suffering from hemorrahge, this treatment was successful.

Ocular Lesions in the Newborn.—LEQUEUX (*Archiv. mensuelle l'Obstétrique*, February, 1912), in examining 151 newborn infants found ocular lesions in 37, or 24.5 per cent. These were paralyses, lesions of the cornea, and lesions of the retina. He also observed 1 case of exophthalmos, 1 of nystagmus, 1 of kemosis, and 1 where there was an abnormal persistence of myelin fibers. The cases of paralysis were those of the seventh pair of cranial nerves, and in 1 case the sixth pair. This followed forceps delivery in difficult labor, with the instru-

ment applied obliquely, one blade over the mastoid region, one over the frontal. Cases where the natural obliquity of the head in labor was lacking comprised the great majority of these. In 2 cases there was paralysis of the seventh and sixth nerves; in 1 the seventh only; in 1 the sixth, and also the roots of the brachial plexus. Lesions of the cornea were most often a cloudiness of varying degree. In some of these cases this disappeared in a short time; in others it persisted for weeks or months. This is usually called traumatic keratitis. It develops in the first twenty-four hours after active labor, often rapidly, and often disappears quickly. In severe cases it may remain. It is usually ascribed to forceps pressure, a blade of the instrument pressing almost directly against the eye. Lequeux found it 6 times, or in 3.9 per cent. of his cases. In 5 of these the lesion disappeared in two or three days; in 1 leukoma resulted; in 3 of the 6 cases forceps were applied, but in 1 of these the instrument was carefully placed over the parietal bones, and direct forceps pressure was absent. Two of the infants were premature. Lequeux believes that this opalescence of the cornea is not infrequent after labor and may readily be overlooked. Direct contusion is not necessary for its production, as the indirect application of force may produce the condition. The pathology of the lesion is obscure and apparently depends upon increase in intra-ocular tension. No treatment is available as most cases recover spontaneously. Retinal lesions were found 15 times, or in 10 per cent. of the cases, most often in both eyes, either at the base of the retina or at other portions. The hemorrhage may extend along the peripheral portion or be circumscribed at the fundus of the retina and choroid. In some cases blood may accumulate between the retina and the vitreus, and may rupture the vitreus. Usually the extravasation is of short duration, leaving minute foci of atrophy in the form of small white dots, which also disappear rapidly. The condition is most often ascribed to contusion and birth pressure in difficult labor with the application of forceps. Lequeux found forceps used in but 12 per cent. of the cases. In breech and shoulder presentations birth pressure is a frequent cause, and the lesion is often accompanied by cerebral hemorrhage or pulmonary apoplexy. It was present in his cases in 14 per cent. of breech extraction; in face presentation the lesion is not infrequent. There seemed to be no difference in the percentage of cases in spontaneous or induced labor, and the accident seemed equally frequent in primiparæ and multiparæ. In 15 cases of contracted pelvis this lesion was present in three infants so born. The weight of the child did not seem to be an essential element, as premature children ill-developed have tissues more liable to hemorrhage than normal infants. There can be no question about the influence of prolonged and difficult labor. Lequeux found an equal proportion of lesions in the anterior and posterior eye. Asphyxia did not seem to be an especially frequent cause of this condition. Blood pressure on the cranium during labor predisposes to this accident. Albuminuria with infarcts in the placenta was also a predisposing cause, and also syphilis. In 6 syphilitic infants, 3 had retinal hemorrhages. Lequeux is impressed with the fact that this condition develops not so frequently from contusion as from intracranial stasis, either papillary stasis from pressure upon the fluid of the cranium and cord, or pressure upon the

venous channels of the cranium and cerebrum. This produces a venous stasis at the border of the retina. Any condition of the blood predisposing to extravasation—as prematurity or syphilis—furthers the development of this condition. One may find the origin of pigmentation of the retina, which is considered a sign of hereditary syphilis, in these retinal hemorrhages.

GYNECOLOGY

UNDER THE CHARGE OF

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Vaccine Diagnosis of Gonorrhea.—STERNBERG (*Gyn. Rundschau*, 1912, vi, 701) says that in treating a large number of cases of inflammatory disease of the uterus and adnexa with gonococcus vaccine, he has found certain clinical manifestations to occur with such regularity in the cases subsequently demonstrated to be of gonorrheal origin that he has come to regard these as of distinct diagnostic value. These manifestations occur usually within a day or two after the first administration of the vaccine, or if this initial dose has been too small, after the next, larger one. They consist, as in practically all forms of immunity reaction, in local, focal, or general disturbances, but in applying gonorrheal vaccine for diagnostic purposes it is desirable as far as possible to avoid local or general reactions, depending upon that at the site of the infection—the focal reaction—to indicate the nature of the condition. For this purpose Sternberg gives an initial dose of 0.3 c.c. of a suspension containing 100,000,000 dead gonococci to the cubic centimeter, injected subcutaneously. If no reaction follows, a few days later a second dose, twice the size of the first, is given. Following this, in gonorrheal cases a marked softening and diminution in tenderness of parametric inflammatory masses and indurated tissue will be noted; the uterus becomes more freely movable, and is much less sensitive to manipulation. If large, tender adnexal masses are present, similar changes occur in these. Sometimes there is a great increase in the amount of discharge, and the next menstrual period may be brought on ahead of time. Increased pain in the pelvic region was complained of only in some cases, and then only for the first day after injection. Control injections of the vaccine have been made on normal individuals, and on those with pelvic masses or indurations of other than gonorrheal origin, without producing any reaction whatever. Especially does this distinction stand out in cases of tubal pregnancy, in which no softening of the mass, or diminution in tenderness, occurs. Sternberg believes, therefore, that this method of diagnosis is of much value, in conjunction with those already in general use.

Treatment of Injured Ureter by Appendiceal Implantation.—The suggestion is made by KENNEDY (*Surg., Gyn., and Obstet.*, 1912, xv, 464) that in cases where the ureter has been resected during operation to such an extent that reimplantation into the bladder is not possible, it would be much better to implant it into the vermiform appendix rather than directly into the colon, or than to do an immediate nephrectomy, the methods which heretofore have been most in vogue in treating this condition. He has found by investigations on dogs and on the cadaver that the appendix is practically always sufficiently movable to permit of the right ureter being implanted into its tip or base with ease, and that unless the appendix or meso-appendix is unusually short, it may be brought far enough over to permit of similar treatment of the left ureter. The advantage claimed by Kennedy for this operation over direct implantation into the gut is the relatively cleaner receptacle offered by the appendix, and therefore the reduced chance of ascending infection. The flow of urine through the appendix will prevent its blockage by fecal concretions, and therefore lessen the risk of inflammation in the organ itself. Moreover, the fold of mucosa at its mouth, known as Gerlach's valve, is far more efficient, even in its most imperfect state of development, than any valve action that can be secured artificially, even by oblique insertion of the ureter into the intestinal walls, thus furnishing still further protection against ascending infection. Before attempting to utilize the appendix, however, the permeability of its lumen must be determined with a probe; even if the distal portion were occluded, this could be resected, and the ureter implanted into the stump.

Normal and Pathological Anatomy of the Endometrium.—In the four years that have elapsed since the publication of Hitchman and Adler's fundamental work on the cyclic changes occurring in the endometrium, numerous investigators have interested themselves in this subject, and most of them have in a general way confirmed the correctness of the main principles laid down by the above-mentioned authors as to the anatomic conditions of the endometrium during the various phases of the menstrual cycle. Practically all subsequent investigations have shown, however, that marked individual variations from these general principles occur. An attempt to simplify and classify the most important of these variations, as reported by various authors, has been made by SCHRODER (*Arch. f. Gyn.*, 1912, xcviii, 81), who tabulates them as follows: (1) Endometria which show a definite cyclic stage, which, however, does not correspond to the clinical stage. (2) Endometria whose anatomical condition does correspond to the clinical stage, but which show hyperplastic processes, such as invagination or clumping of glands. (3) Endometria which show the anatomic characteristics of several different stages. (4) Endometria which, taken from the ninth to the fourteenth day, show a condition corresponding to the end of menstruation. (5) Endometria which always show one definite gland type, no matter in what period of the menstrual cycle the examination is made. Schröder has examined with great care the endometrium from 205 patients, in all of whom the exact date of the preceding menstruation, and the menstrual type, was known. The specimens were obtained

in part from extirpated uteri, in part by curettage. In 120 of these cases, or 66 per cent., the anatomic picture presented by the endometrium corresponded with the clinical stage at which it was removed; in 22 cases the endometrium presented a uniform anatomic picture, but this corresponded either to an earlier or a later stage than that actually presented by the patient. In all the remaining cases the structure of the endometrium showed variations from the normal, and these have been therefore classed as "pathological" (entirely irrespective of the presence or absence of inflammatory changes). These cases all fall into one of three groups: (1) Endometria which show side by side the characteristics of several stages. (2) Endometria which show diffuse or localized stroma changes without variations in the gland picture. (3) Endometria presenting the picture of glandular or glandular-cystic hyperplasia. Schröder believes that these conditions are all due to disturbances in ovarian function, and has not found any reason to consider inflammatory conditions responsible for them. In the diagnosis of inflammation Schröder depends almost entirely on the round cell and plasma-cell content of the endometrium. He considers a diffuse distribution of round cells throughout the stroma in moderate numbers, and even a moderate amount of grouping of these into small foci, to be a normal occurrence, as is a scattering of plasma cells. As soon, however, as the round cell-groups become larger and more numerous, and the plasma-cell content richer, he considers inflammation to be present, but recognizes that this distinction must be largely subjective. He thinks that no diagnostic value can be placed upon the presence of either edema or hemorrhage, since both may occur purely as the result of operative trauma. The presence of inflammation does not, as a rule, seem to affect the regular cyclic evolution and involution of the endometrium, a point which has been especially brought out by Schröder's investigations being the great persistency in maintaining these cyclic changes exhibited by the endometrium, even in the presence of serious pathological conditions.

Treatment of Incontinence of Urine in Women.—Caspar (*Zeitsch. f. Urologie*, 1912, II Beiheft, 238) reports 2 cases of incontinence of urine in women due to stretching or trauma of the urethra and surrounding tissue, in which numerous methods of cure had been tried without success. He was able to produce complete cure in each instance by cauterization of the internal vesical sphincter. The operation is performed through Caspar's operating cystoscope, two or three deep grooves being burned in the sphincter at the point of transit from the bladder to the urethra. This causes scar-formation, and resulting contraction of the sphincter apparatus, which should in most cases be sufficient to produce complete continence, although in some conditions, as for instance, where an extensive prolapse of the anterior vaginal wall is constantly pulling on the sphincter and stretching it, it probably would not be successful. The operation is easy of performance with the proper instrument, and free from danger, and should, Caspar thinks, form a useful addition to our resources in the treatment of what is often an extremely baffling condition. He has also tried it in one case of stubborn eneuresis nocturna in a girl, aged sixteen years, likewise with complete success.

DERMATOLOGY

UNDER THE CHARGE OF

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Some Physicotherapeutic Methods in Dermatology.—MALCOLM MORRIS (*British Jour. of Derm.*, May, 1912), in an interesting short article gives his experience with some of the newer methods employed in a number of obstinate diseases. His conclusions may be summarized as follows: The *x*-rays, radium, Finsen light, and freezing with carbon dioxide snow, are serviceable in the highest degree in early rodent ulcer, in tinea tonsurans, tinea sycosis, and tinea favosa, also in lupus vulgaris and small tuberculous glands, in lupus erythematosus, in certain kinds of nævi, in scars, and in keloid. In these diseases they are superior to medicine, the knife, or to any other form of surgical treatment. They are valuable in a somewhat less degree in later rodent ulcer, and in superficial carcinoma. They are serviceable in varying degrees, in coccogenic sycosis, in hyperidrosis, in hypertrichosis, in chronic eczema, pruritus, and lichenification, and in papilloma, while they possess distinct alleviative influence in such grave affections as Paget's disease, deep-seated carcinoma, sarcoma, mycosis fungoides, and leprosy.

New Method of Removing Superfluous Hairs.—W. SCHWENTER-TRACHSLER (*Jour. of Cut. Dis.*, June, 1912, p. 364) refers to 252 cases in which she has employed the following method with success. After removing the entire growth (by shaving ?) the patient rubs pumice stone in twice daily, under which procedure the hair is prevented from coming to the surface, and if this rubbing be persisted in for a year, atrophy of the follicles occurs and finer hairs or no hairs. The skin is never injured by this treatment.

Treatment of Itching Skin Diseases with Normal Human Serum.—LINSEN (*Dermatol. Woch.*, March 30, 1912), quotes a case of impetigo herpetiformis in which a cure followed the injection of serum taken from a normal pregnant woman. This treatment was also employed successfully in other dermatoses associated with pregnancy, and in other itching diseases of the skin, with favorable results, as urticaria, especially in infants, prurigo, and infantile eczema. Good results were obtained in senile pruritus in cases where no benefit had followed saline injections. In generalized eczema in adults favorable results were also obtained. The serum of a healthy pregnant woman is to be used,

that of a non-pregnant woman not proving satisfactory. For females the serum of females and for males that of males should be made use of. The fresher the serum the better. Fifty cubic centimeters of blood are withdrawn from the arm into a sterile centrifugalizing tube containing glass beads, the blood is defibrinated by shaking for five minutes. The serum is separated in the centrifugal machine, sucked up with a sterile syringe, and injected into a vein. In children it is injected subcutaneously. The dose is from 10 to 20 c.c., repeated on successive days, three to five injections being given. The treatment may be used in dispensary practice.

A Useful Formula for the Widespread Tinea Tonsurans.—A. W. WILLIAMS (*British Jour. of Derm.*, June, 1912) has used the following formula in a number of cases, and finds it to be remarkably efficacious. It consists of camphor, alcohol, āā ℥iv; picric acid, gr. vii. *Sig.*, Inflammable; paint all over scalp twice daily. An objection to its use is the yellow staining of the hair, which is still noticeable three weeks after stopping the treatment. Camphor and alcohol without the picric acid do not appear to be effective.

Pemphigus Foliaceus.—H. H. HAZIN (*Jour. of Cutan. Dis.*, June, 1912) cites a case of this disease in an adult, and also gives the notes of a case of dermatitis exfoliative neonatorum in a child, aged fourteen days, and then discusses the relation of these two diseases, concluding that some cases of pemphigus foliaceus are undoubtedly due to a Bacillus pyocyaneous infection, and that the name dermatitis exfoliativa neonatorum is not a suitable one, as the exfoliation is secondary to a generalized cutaneous infection, probably with the Staphylococcus albus. The two diseases are different, though there may be gradations between them.

Concerning the So-called Lichen Albus of Zumbusch.—VIGNOLO-LUTATI (*Dermat. Woch.*, June 8, 1912) gives a case and enters upon the pathological anatomy of the lesions (with microphotographs), and concludes from a study of the literature and his own case, that he is forced to agree with the views already published by Hallopeau, that the affection must be regarded as a type of the sclerous form of lichen of Wilson, and that it is inappropriate to designate it with the new name of "white lichen," which term, moreover, is not exact, since the lesion may be in the beginning, bright red. Under the name of "white spot disease" cases of probably the same disease have been reported of late years by various writers.

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All communications should be addressed to—

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AND

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